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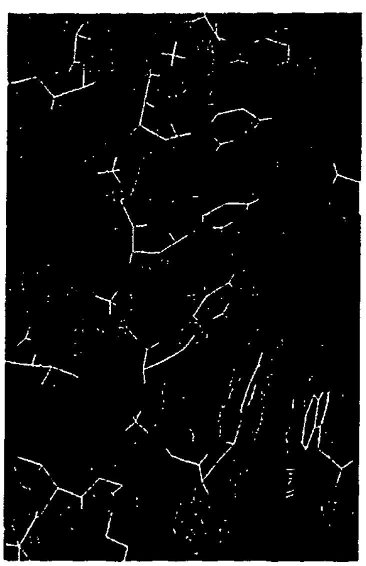

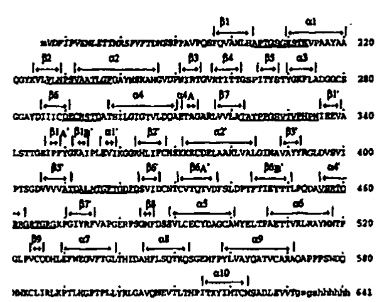

(57) Abstract

The invention relates to the X–ray crystal structure of the hepatitis C virus helicase domain. More specifically, the invention relates to crystallized complexes of HCV helicase and an oligonucleotide, to crystallizable compositions of HCV helicase and an oligonucleotide and to methods of crystallizing an HCV helicase–oligonucleotide complex. The invention further relates to a computer programmed with the structure coordinates of the HCV helicase oligonucleotide binding pocket or the HCV helicase nucleotide triphosphate pocket wherein said computer is capable of displaying a three–dimensional representation of that binding pocket.

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CRYSTALS OF HEPATITIS C VIRUS HELICASE OR FRAGMENTS THEREOF COMPRISING A HELICASE BINDING POCKET

TECHNICAL FIELD OF THE INVENTION

The invention relates to the X-ray crystal structure of the hepatitis C virus helicase domain. More specifically, the invention relates to crystallized complexes of HCV helicase and an oligonucleotide, to crystallizable compositions of HCV helicase and an oligonucleotide and to methods of crystallizing an HCV helicase-oligonucleotide complex. The invention further relates to a computer programmed with the structure coordinates of the HCV helicase oligonucleotide binding pocket or the HCV helicase nucleotide triphosphate pocket wherein said computer is capable of displaying a three-dimensional representation of that binding pocket.

BACKGROUND OF THE INVENTION

Infection by the hepatitis C virus (HCV) is responsible for most transfusion-associated cases of non-A, non-B hepatitis and also accounts for a significant proportion of community-acquired hepatitis cases worldwide. Relatively few HCV infected individuals

experience acute hepatitis, but up to 85% appear to develop persistent infection that often leads to chronic hepatitis and liver cirrhosis, eventually predisposing them to hepatocellular carcinoma. At present, vaccines are unavailable and no broadly effective therapies exist for this viral disease. Consequently, much research has focused on the HCV replicative enzymes as targets for more effective therapies.

HCV contains an approximately 9.6 kb single-stranded positive sense RNA genome classified as its own genus in the *Flaviviridae* family of animal viruses, which also includes the flavivirus and pestivirus genera. Its genome consists of a conserved 5' nontranslated sequence that serves as an internal ribosome entry site, a single open reading frame that encodes a polyprotein of >3000 amino acids, and a 3' nontranslated region. The 3' nontranslated region contains tracts of poly(U)$_n$ and poly(UC)$_n$ followed by a novel conserved 98 nucleotide sequence.

Proteolytic processing of the HCV polyprotein by virally-encoded proteases generates several nonstructural (NS) proteins with enzymatic activities essential for the replicative cycle of the virus [P. Neddermann et al., Biol. Chem., 378, pp. 469-476 (1997)].

NS2 encodes a presumed metalloprotease, NS5B is a RNA-dependent RNA polymerase, and NS3 is a bifunctional enzyme with a serine protease localized to the N-terminal 181 residues of the protein and a RNA helicase in the C-terminal 465 amino acids. The NS3 protease performs an intramolecular cleavage at the NS3/NS4A junction to form a tight noncovalent NS3-NS4A complex necessary for efficient processing of the remaining polyprotein [C. Failla et al., J. Virol., 69, pp. 1769-1777 (1995); R. Bartenschlager et al., J. Virol., 69, pp. 7519-7528 (1995); Y. Tanji et al., J. Virol., 69, pp. 1575-1581 (1995)]. To date, no evidence exists to suggest that the serine protease and helicase domains are separated by proteolytic processing of NS3 in vivo. This may reflect economical packaging of these enzymatic components, or could imply a functional interdependence between the two domains.

Numerous studies have demonstrated that the serine protease [J. L. Kim et al., Cell, 87, pp. 343-355 (1996); W. Markland et al., J. Gen. Virol., 78, pp. 39-43(1997).; C. Steinkuhler et al., J. Virol., 70, pp. 6694-6700 (1996)] and RNA helicase domains [J. A. Suzich et al., J. Virol., 67, pp. 6152-6158 (1993); C. L. Tai et al., J. Virol., 70, pp. 8477-8484 (1996); L. Jin et al.,

Arch. Biochem. Biophys., 323, pp. 47-53 (1995); and F. Preugschat et al., J. Biol. Chem., 271, pp. 24449-24457 (1996)] of NS3 can be expressed independently and isolated as catalytically active species. However, emerging evidence suggests that the NS3 protease and helicase domains may contact one another and modulate NS3 catalytic activities. Examples include apparent differences in pH optima of ATPase and RNA unwinding activities between a contiguous NS3 protein complexed with the NS4A cofactor [K. A .Morgenstern et al., J. Virol., 71, pp. 3767-3775 (1997); Z. Hong et al., J. Virol., 70, pp. 4261-4268 (1996)] and an isolated NS3 helicase domain [C. L. Tai et al., J. Virol., (1996), supra; L. Jin et al., Arch. Biochem. Biophys., (1995), supra; F. Preugschat et al., J. Biol. Chem., (1996), supra; and Y. Gwack et al., Biochem. Biophys. Res. Commun., 225, pp. 654-659 (1996)]. Similarly, the ATPase activities of both proteins differ in their sensitivity to polynucleotide stimulation. Contiguous NS3 appears to have a lower apparent dissociation constant for poly(U) than does the helicase domain [J. A. Suzich et al., J. Virol., (1993), supra; F. Preugschat et al., J. Biol. Chem., (1996), supra; K. A .Morgenstern et al., J. Virol., (1997), supra; A. Kanai et al., FEBS Lett., 376,

pp. 221-224 (1995)]. Aside from these differences, both proteins display nearly indistinguishable kinetic parameters for NTP hydrolysis when stimulated with saturating polynucleotide [J. A. Suzich et al., J. Virol., (1993), supra; K. A .Morgenstern et al., J. Virol., (1997), supra], both display 3′- 5′ directionality for translocation along a polynucleotide substrate, and the helicases of both proteins effectively unwind duplex RNA:RNA substrates [C. L. Tai et al., J. Virol., (1996), supra; Z. Hong et al., J. Virol., (1996), supra].

In addition to HCV, all flavi- and pestiviruses sequenced to date contain conserved helicase sequence motifs in their homologous NS3 proteins, suggesting that this enzyme plays an important role in the HCV replicative cycle [R. H. Miller et al., Proc. Natl. Acad. Sci. USA, 87, pp. 2057-2061 (1990)]. Consistent with this possibility, helicase encoding sequences have been identified in other viruses and helicases are suggested to catalyze the separation of double-stranded nucleic acid structures during transcription and genome replication [G. Kadare et al., J. Virol., 71, pp. 2583-2590 (1997)]. Previous studies with poliovirus, a positive-stranded RNA virus of the *Picornaviridae* family,

show that mutation of conserved sequence motifs in the 2C helicase inhibits virus replication and proliferation [C. Mirzayan et al., Virology, 189, pp. 547-555 (1992)]. Similar mutational studies on the helicases encoded by herpes simplex virus type 1 and bovine papilloma virus also show that these enzymes are critical for virus replication [P. MacPherson et al., Virology, 204, pp. 403-408 (1994); R. Martinez et al., J. Virol., 66, pp. 6735-6746 (1992)]. Thus, the ability to inhibit helicase activity in HCV may provide an avenue for the therapeutic treatment of HCV infection.

Unfortunately, little is known about the details of how ATP binding and hydrolysis leads to DNA or RNA strand unwinding by the helicase. Two structures of helicases crystallized in the absence of polynucleotide, but, unfortunately, they have not yielded the critical information needed to extrapolate to an enzyme mechanism [N. Yao et al., Nat. Struct. Biol., 4, pp. 463-467 (1997); H. S. Subramanya et al., Nature, 384, pp. 379-383 (1996)].

Thus, there is a great need to solve the crystal structure of the helicase complexed with an oligonucleotide and, in particular, to delineate the oligonucleotide and nucleotide triphosphate (NTP) binding

pockets of that enzyme. With this information, computer models of these binding sites can be created and potential inhibitors of HCV helicase can be rationally designed.

SUMMARY OF THE INVENTION

Applicants have solved this problem by providing a crystallized complex of the NS3 helicase domain of HCV and a single stranded oligonucleotide. That crystal has been solved by X-ray crystallography to a resolution of 2.2Å. Based upon that crystal structure, applicants have identified the key amino acid residues that make up the oligonucleotide binding pocket of the helicase.

Thus, the invention relates to a crystallized complex comprising the NS3 helicase domain of hepatitis C virus or mutants thereof and an oligonucleotide.

The invention also relates to crystallizable compositions comprising the NS3 helicase domain, either as an isolated polypeptide or as part of the full length NS3 HCV protein, or single amino acid mutants thereof, and an oligonucleotide. And it relates to methods of using such compositions to produce the aforementioned crystals.

The invention also provides the X-ray structure coordinates of an NS3 helicase-oligonucleotide complex. Those coordinates, or at least the portion that define the oligonucleotide binding pocket or the NTP binding pocket are useful in methods for designing inhibitors of the NS3 helicase, which in turn may be useful in treating HCV infection. This is another aspect of the present invention.

In a related aspect, the invention provides a computer programmed with the coordinates of the NS3 helicase oligonucleotide binding pocket or the NTP binding pocket and with a program capable of converting those coordinates into a three-dimensional representation of the binding pocket on a display connected to the computer.

Finally, the invention provides a computer which, when programmed with at least a portion of the structural coordinates of HCV NS3 helicase and an X-ray diffraction data set of a different molecule or molecular complex, performs a Fourier transform of these structural coordinates of the helicase coordinates and then processes the X-ray diffraction data into structure coordinates of the different molecule or molecular complex via the process of molecular replacement.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 lists the atomic structure coordinates for NS3 helicase in complex with dU_8 as derived by X-ray diffraction from a crystal of that complex. The following abbreviations are used in Figure 1:

"Atom type" refers to the element whose coordinates are measured. The first letter in the column defines the element.

"X, Y, Z" crystallographically define the atomic position of the element measured.

"B" is a thermal factor that measures movement of the atom around its atomic center.

"Occ" is an occupancy factor that refers to the fraction of the molecules in which each atom occupies the position specified by the coordinates. A value of "1" indicates that each atom has the same conformation, i.e., the same position, in all molecules of the crystal.

Figure 2 shows a diagram of a computer used to generate a three-dimensional graphical representation of a molecule or molecular complex according to this invention.

Figure 3 shows a cross section of a magnetic storage medium.

Figure 4 shows a cross section of a optically-readable data storage medium.

Figure 5 depicts a stereo ribbon diagram of the overall fold of the NS3 helicase with bound $d(U)_8$. Domain 1 is colored blue, domain 2 red, and domain 3 green. The sulfate and DNA are colored yellow.

Figure 6 depicts a superposition of domains 1 (blue) and 2 (red) of NS3 helicase based on conserved secondary structure motifs with a 2.0 Å C-alpha RMS deviation over 78 residues. Residues corresponding to binding to the 3' end of the oligonucleotide are depicted as thick lines. Also shown is the location of Trp-501.

Figure 7, panel A, depicts the residues surrounding the bound sulfate superimposed on the phosphate binding loops of eight deoxynucleoside monophosphate kinases. Panel B depicts the electron density encompassing the bound DNA substrate. The orange color depicts the difference Fourier (F_O-F_C) electron density map calculated before DNA or water molecules were built into the model. The blue color depicts the final $2F_O$-F_C electron density map calculated at 2.2Å resolution using the refined model.

Figure 8 depicts the secondary structure of HCV NS3 helicase (indicated above the sequence). The

conserved sequence motifs are underscored. The non-HCV N-terminal and C-terminal residues which were added during cloning are depicted in lower case. No density was observed for residues in italics. The residues are numbered based on their location in the NS3 protein.

Figure 9, panel A, depicts aligned sequences of conserved motifs from other helicases. The motifs are colored similar to what was previously reported for the PcrA helicase to aid in comparison of the structures of enzymes from superfamilies I and II. Panel B depicts the location of conserved motifs.

Figure 10 depicts a view into the central binding cleft of the NS3 helicase domain.

Figure 11, Panel A, depicts the effect of enzyme concentration and incubation time on HCV NS3 helicase. Panel B depicts the effect of incubation temperature on helicase activity. Panel C depicts the effect of pH on helicase activity. Panel D depicts the effect of monovalent cations on helicase activity. Panel E depicts the effect of ATP on helicase activity. Panel F depicts the effect of divalent cations on enzyme activity.

Figure 12, Panel A depicts the effect of enzyme concentration on the binding of [^{32}P]-ssRNA substrate to

HCV NS3 helicase. Panel B depicts the dissociation of pre-formed NS3 helicase/ [^{32}P]-labeled ssRNA complex by [^{3}H] -labeled ssRNA over time. Panel C depicts the effect of pH on the binding of ssRNA to helicase. Panel D depicts the effect of monovalent cation on ssRNA binding to helicase. Panel E depicts the effect of divalent cations on ssRNA binding to helicase.

Figure 13 Panel A depicts the effect of poly (U) on the ATPase activity of HCV NS3 helicase. Panel B depicts the effect of enzyme concentration on ATPase activity in the presence or absence of poly (U).

DETAILED DESRIPTION OF THE INVENTION

In order that the invention described herein may be more fully understood, the following detailed description is set forth.

According to one embodiment, the invention provides a crystallizable composition comprising NS3 helicase and an oligonucleotide.

The NS3 helicase protein in the crystallizable complexes of this invention is selected from the isolated helicase domain from any strain or the consensus sequence of the HCV NS3 protein (e.g., amino acids 167-631 of SEQ

ID NO:2); the entire NS3 protein from any strain of HCV or the consensus sequence of that protein (e.g., SEQ ID NO:2); any portion of the NS3 protein that contains a functional helicase domain, which has been indicated to be amino acids 183-582 by C. Hyun-Soo et al., J. Biol. Chem., 273, pp. 15045-15052 (1998), from any strain of HCV or the consensus sequence of that protein (e.g., amino acids 183-582 of SEQ ID NO:2, amino acids 167-631 of SEQ ID NO:2, amino acids 183-631 of SEQ ID NO:2) and amino acid mutants of any of the above (including, but not limited to, SEQ ID NO:2 or any portion thereof that includes amino acids 183-582 of SEQ ID NO:2 and contains one or more of the following single amino acid replacements: Ser231-to-Ala, Thr269-to-Ala, Ser370-to-Ala, Thr411-to-Ala, Trp501-to-Phe, Trp501-to-Leu or Trp501-to-Ala, Gln460-to-Ala, Arg461-to-Ala, Arg462-to-Ala, Arg464-to-Ala, or Arg467-to-Ala).

The NS3 protein utilized in the crystallizable compositions of this invention may also contain additional amino acids at the N- and/or C-terminus which may be useful in purifying the protein when produced recombinantly. For example, we have found that a poly-histidine tag at the C-terminus is useful in purifying NS3 proteins produced in recombinant host cells through

the use of appropriate resins, such as Q-Sepharose (Pharmacia, Piscataway, NJ). Such tags may also be useful in increasing the solubility of the NS3 protein.

The second component in these compositions is an oligonucleotide. Preferably, the oligonucleotide is single-stranded, although double-stranded oligonucleotides may be used and subsequently dissociated prior to crystallization. Preferably, the oligonucleotide is a polynucleotide of between about 6 and 20 bases. More preferably, the oligonucleotide is between about 6 and 12 bases. Most preferably, the oligonucleotide is polyuracil 8 nucleotides long (dU_8).

The molar ratio of NS3 helicase to oligonucleotide should be about 1:1, although ranges between 1:5 and 5:1 are acceptable.

The buffers and other reagents present in the crystallizable compositions of this application may be any components that promote crystallization and/or are compatible with crystallization conditions. An example of such a buffer condition is 15 mM MES (pH 6.5), 2.5 mM ß-mercaptoethanol.

The invention also relates to crystals of NS3 helicase complexed with an oligonucleotide. Both the NS3 helicase component and the oligonucleotide component are

the same as those described above for crystallizable compositions. These crystals are obtained from the above described compositions by standard crystallization protocols, such as the protocol exemplified in the Example section below.

The invention also relates to a method of making NS3 helicase-containing crystals. Such methods comprise the steps of:

a) obtaining a crystallizable composition comprising an NS3 helicase protein and an oligonucleotide in a molar ratio of between 1:5 and 5:1; and

b) subjecting said composition to conditions which promote crystallization.

Again, the choice for the NS3 helicase protein and the oligonucleotide utilized in the above crystallization method are the same as those set forth above for crystallizable compositions.

As mentioned above, applicants have solved the three-dimensional X-ray crystal structure of an NS3 helicase-dU_8 complex. The atomic coordinate data is presented in Figure 1.

In order to use the structure coordinates generated for the NS3 helicase-dU_6 complex or its NTP or oligonucleotide binding pockets or portions or homologues

thereof, it is often times necessary to convert them into a three-dimensional shape. This is achieved through the use of commercially available software that is capable of generating three-dimensional graphical representations of molecules or portions thereof from a set of structure coordinates.

Binding pockets, also referred to as binding sites in the present invention, are of significant utility in fields such as drug discovery. The association of natural ligands or substrates with the binding pockets of their corresponding receptors or enzymes is the basis of many biological mechanisms of action. Similarly, many drugs exert their biological effects through association with the binding pockets of receptors and enzymes. Such associations may occur with all or any parts of the binding pocket. An understanding of such associations will help lead to the design of drugs having more favorable associations with their target receptor or enzyme, and thus, improved biological effects. Therefore, this information is valuable in designing potential inhibitors of the binding sites of biologically important targets.

The term "binding pocket", as used herein, refers to a region of a molecule or molecular complex,

that, as a result of its shape, favorably associates with another chemical entity or compound.

Applicants have identified three binding pockets which are good targets for designing inhibitors. Two of these binding pockets reside in the region of the helicase where an oligonucleotide binds. These pockets are designated U4 and U8, based upon the nucleotide of dU_8 that lies in this pocket in an NS3 helicase-dU_8 complex. The third binding pocket is the NTP binding pocket. While this binding pocket has been partially described by others [T. Yao et al., Nat. Struct. Biol., 4, pp. 463-467 (1997)], applicants have further defined this pocket in a way that was not derivable from what was known in the art.

The terms "U4-, U8- and NTP-like binding pocket", as used herein, refer to a portion of a molecule or molecular complex whose shape is sufficiently similar to the NS3 helicase U4, U8 and NTP binding pocket, so as to bind common ligands. These commonalties of shape are defined by a root mean square deviation from the structure coordinates of the backbone atoms of the amino acids that make up these binding pockets in the NS3 helicase structure (as set forth in Figure 1) of not more

than 1.5 Å. The method of performing this calculation is described below.

In resolving the crystal structure of NS3 helicase in complex with an oligonucleotide, applicants have determined that NS3 amino acids Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501 and Tyr502 form close contacts (<4Å) with U8 of dU_8 in the NS3 helicase-dU_8 complex. Thus, a binding pocket defined by the structural coordinates of those amino acids, as set forth in Figure 1; or a binding pocket whose root mean square deviation from the structure coordinates of the backbone atoms of those amino acids of not more than 1.5 Å is considered a U8-like binding pocket of this invention.

Applicants have also determined that in addition to the NS3 amino acids set forth above, Pro230, Val256, Thr298, Ala497, Lys551, Gln552, Gly554, Glu555, Asn556 and Pro558 are within 8Å of U8 of the bound oligonucleotide and therefore are also close enough to interact with that substrate. Thus, in a preferred embodiment, a binding pocket defined by the structural coordinates of the amino acids that are within 8Å of U8 of the bound oligonucleotide, as set forth in Figure 1; or a binding pocket whose root mean square deviation from the structure coordinates of the backbone atoms of those

amino acids is not more than 1.5 Å is considered a preferred NS3 helicase U8-like binding pocket of this invention.

Applicants have further determined that the NS3 helicase amino acids that define the shape of the U4 oligonucleotide binding pocket are: His369, Ser370, Lys371, Tyr392, Arg393, Thr411, Asp412, Ala413, Cys431, Val432, Gln434, Ile446, Thr448, Arg461, Glu493, Glu555, Asn556 and Phe557. Thus, a binding pocket defined by the structural coordinates of these amino acids, as set forth in Figure 1; or a binding pocket whose root mean square deviation from the structure coordinates of the backbone atoms of these amino acids is not more than 1.5 Å is considered a NS3 helicase U4-like binding pocket of this invention.

Applicants have also more completely determined, as compared to the prior art, the NS3 helicase amino acids that define the shape of the NTP binding pocket. Those amino acids are: Pro205, Thr206, Gly207, Ser208, Gly209, Lys210, Ser211, Thr212, Lys213, Asn229, Ala234, Gly237, Phe238, Tyr241, Asp290, Glu291, His293, Thr322, Ala323, Thr324, Gln460, Gly463, Arg464 and Arg467. Thus, a binding pocket defined by the structural coordinates of these amino acids, as set forth

in Figure 1; or a binding pocket whose root mean square deviation from the structure coordinates of the backbone atoms of these amino acids is not more than 1.5 Å is considered a NS3 helicase NTP-like binding pocket of this invention.

It will be readily apparent to those of skill in the art that the numbering of amino acids in other isoforms of NS3 may be different than that set forth for herein. Corresponding amino acids in other isoforms of NS3 are easily identified by visual inspection of the amino acid sequences or by using commercially available homology software programs.

Each of those amino acids of NS3 helicase is defined by a set of structure coordinates set forth in Figure 1. The term "structure coordinates" refers to Cartesian coordinates derived from mathematical equations related to the patterns obtained on diffraction of a monochromatic beam of X-rays by the atoms (scattering centers) of a protein or protein-ligand complex in crystal form. The diffraction data are used to calculate an electron density map of the repeating unit of the crystal. The electron density maps are then used to establish the positions of the individual atoms of the enzyme or enzyme complex.

Those of skill in the art understand that a set of structure coordinates for an enzyme or an enzyme-complex or a portion thereof, is a relative set of points that define a shape in three dimensions. Thus, it is possible that an entirely different set of coordinates could define a similar or identical shape. Moreover, slight variations in the individual coordinates will have little effect on overall shape. In terms of binding pockets, these variations would not be expected to significantly alter the nature of ligands that could associate with those pockets.

The term "associating with" refers to a condition of proximity between a chemical entity or compound, or portions thereof, and a binding pocket or binding site on a protein. The association may be non-covalent -- wherein the juxtaposition is energetically favored by hydrogen bonding or van der Waals or electrostatic interactions -- or it may be covalent.

The variations in coordinates discussed above may be generated because of mathematical manipulations of the NS3 helicase-oligonucleotide complex structure coordinates. For example, the structure coordinates set forth in Figure 1 could be manipulated by crystallographic permutations of the structure

coordinates, fractionalization of the structure coordinates, integer additions or subtractions to sets of the structure coordinates, inversion of the structure coordinates or any combination of the above.

Alternatively, modifications in the crystal structure due to mutations, additions, substitutions, and/or deletions of amino acids, or other changes in any of the components that make up the crystal could also account for variations in structure coordinates. If such variations are within an acceptable standard error as compared to the original coordinates, the resulting three-dimensional shape is considered to be the same. Thus, for example, a ligand that bound to the oligonucleotide binding pocket of NS3 helicase would also be expected to bind to another binding pocket whose structure coordinates defined a shape that fell within the acceptable error.

Various computational analyses are therefore necessary to determine whether a molecule or the binding pocket portion thereof is sufficiently similar to the NS3 helicase binding pockets described above. Such analyses may be carried out in well known software applications, such as the Molecular Similarity application of QUANTA

(Molecular Simulations Inc., San Diego, CA) version 4.1, and as described in the accompanying User's Guide.

The Molecular Similarity application permits comparisons between different structures, different conformations of the same structure, and different parts of the same structure. The procedure used in Molecular Similarity to compare structures is divided into four steps: 1) load the structures to be compared; 2) define the atom equivalences in these structures; 3) perform a fitting operation; and 4) analyze the results.

Each structure is identified by a name. One structure is identified as the target (i.e., the fixed structure); all remaining structures are working structures (i.e., moving structures). Since atom equivalency within QUANTA is defined by user input, for the purpose of this invention we will define equivalent atoms as protein backbone atoms (N, Cα, C and O) for all conserved residues between the two structures being compared. We will also consider only rigid fitting operations.

When a rigid fitting method is used, the working structure is translated and rotated to obtain an optimum fit with the target structure. The fitting operation uses an algorithm that computes the optimum

translation and rotation to be applied to the moving structure, such that the root mean square difference of the fit over the specified pairs of equivalent atom is an absolute minimum. This number, given in angstroms, is reported by QUANTA.

For the purpose of this invention, any molecule or molecular complex or binding pocket thereof that has a root mean square deviation of conserved residue backbone atoms (N, Cα, C, O) of less than 1.5 Å when superimposed on the relevant backbone atoms described by structure coordinates listed in Figure 1 are considered identical. More preferably, the root mean square deviation is less than 1.0Å.

The term "root mean square deviation" means the square root of the arithmetic mean of the squares of the deviations from the mean. It is a way to express the deviation or variation from a trend or object. For purposes of this invention, the "root mean square deviation" defines the variation in the backbone of a protein from the backbone of NS3 helicase or a binding pocket portion thereof, as defined by the structure coordinates of NS3 helicase described herein.

Therefore, according to another embodiment of this invention is provided a computer for producing:

a) a three-dimensional representation of a molecule or molecular complex, wherein said molecule or molecular complex comprises a binding pocket defined by structure coordinates of NS3 amino acids Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501 and Tyr502 according to Figure 1; or

b) a three-dimensional representation of a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, wherein said computer comprises:

(i) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said data comprises the structure coordinates of NS3 amino acids Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501 and Tyr502 according to Figure 1;

(ii) a working memory for storing instructions for processing said machine-readable data;

(iii) a central-processing unit coupled to said working memory and to said machine-readable data storage medium for processing said machine readable data into said three-dimensional representation; and

(iv) a display coupled to said central-processing unit for displaying said three-dimensional representation.

According to a preferred embodiment, the computer produces a three-dimensional representation of:

a) a molecule or molecular complex comprising a binding pocket defined by the structure coordinates of NS3 helicase amino acids Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501, Tyr502, Pro230, Val256, Thr298, Ala497, Lys551, Gln552, Gly554, Glu555, Asn556 and Pro558, according to Figure 1; or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å. In that preferred embodiment, the machine readable data comprises the structure coordinates of NS3 amino acids Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501, Tyr502, Pro230, Val256, Thr298, Ala497, Lys551, Gln552, Gly554, Glu555, Asn556 and Pro558, according to Figure 1.

In the above two embodiments, the computer is producing a three-dimensional graphical structure of a

molecule or a molecular complex which comprises a NS3 helicase U8-like binding pocket.

In an alternate embodiment, the computer produces a three-dimensional representation of:

a) a molecule or molecular complex comprising a binding pocket defined by the structure coordinates of NS3 helicase amino acids His369, Ser370, Lys371, Tyr392, Arg393, Thr411, Asp412, Ala413, Cys431, Val432, Gln434, Ile446, Thr448, Arg461, Glu493, Glu555, Asn556 and Phe557, according to Figure 1; or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å

In this alternate embodiment, the machine readable data comprises the structure coordinates of NS3 amino acids His369, Ser370, Lys371, Tyr392, Arg393, Thr411, Asp412, Ala413, Cys431, Val432, Gln434, Ile446, Thr448, Arg461, Glu493, Glu555, Asn556 and Phe557, according to Figure 1.

In this embodiment, the computer is producing a three-dimensional graphical structure of a molecule or a molecular complex which comprises a NS3 helicase U4-like binding pocket.

In yet another alternate embodiment, the computer produces a three-dimensional representation of:

a) a molecule or molecular complex comprising a binding pocket defined by the structure coordinates of NS3 helicase amino acids Pro205, Thr206, Gly207, Ser208, Gly209, Lys210, Ser211, Thr212, Lys213, Asn229, Ala234, Gly237, Phe238, Tyr241, Asp290, Glu291, His293, Thr322, Ala323, Thr324, Gln460, Gly463, Arg464 and Arg467, according to Figure 1; or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å

In this alternate embodiment, the machine readable data comprises the structure coordinates of NS3 amino acids Pro205, Thr206, Gly207, Ser208, Gly209, Lys210, Ser211, Thr212, Lys213, Asn229, Ala234, Gly237, Phe238, Tyr241, Asp290, Glu291, His293, Thr322, Ala323, Thr324, Gln460, Gly463, Arg464 and Arg467, according to Figure 1.

In this embodiment, the computer is producing a three-dimensional graphical structure of a molecule or a molecular complex which comprises a NS3 helicase NTP-like binding pocket.

Even more preferred is a computer for producing a three-dimensional representation of a molecule or molecular complex defined by structure coordinates of all of the NS3 amino acids set forth in Figure 1, or a three-dimensional representation of a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å. In this embodiment, the machined readable data contains the coordinates of all of the NS3

According to an alternate embodiment, the invention provides a computer for determining at least a portion of the structure coordinates corresponding to X-ray diffraction data obtained from a molecule or molecular complex, wherein said computer comprises:

(a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said data comprises at least a portion of the structural coordinates of NS3 helicase according to Figure 1;

(b) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said data comprises X-ray diffraction data from said molecule or molecular complex;

(c) a working memory for storing instructions for processing said machine-readable data of (a) and (b);

(d) a central-processing unit coupled to said working memory and to said machine-readable data storage medium of (a) and (b) for performing a Fourier transform of the machine readable data of (a) and for processing said machine readable data of (b) into structure coordinates; and

(e) a display coupled to said central-processing unit for displaying said structure coordinates of said molecule or molecular complex.

For example, the Fourier transform of the structure coordinates set forth in Figure 1 may be used to determine at least a portion of the structure coordinates of other helicases.

Figure 2 demonstrates one version of these embodiments. System 10 includes a computer 11 comprising a central processing unit ("CPU") 20, a working memory 22 which may be, e.g., RAM (random-access memory) or "core" memory, mass storage memory 24 (such as one or more disk drives or CD-ROM drives), one or more cathode-ray tube ("CRT") display terminals 26, one or more keyboards 28, one or more input lines 30, and one or more output lines

40, all of which are interconnected by a conventional bi-directional system bus 50.

Input hardware 36, coupled to computer 11 by input lines 30, may be implemented in a variety of ways. Machine-readable data of this invention may be inputted via the use of a modem or modems 32 connected by a telephone line or dedicated data line 34. Alternatively or additionally, the input hardware 36 may comprise CD-ROM drives or disk drives 24. In conjunction with display terminal 26, keyboard 28 may also be used as an input device.

Output hardware 46, coupled to computer 11 by output lines 40, may similarly be implemented by conventional devices. By way of example, output hardware 46 may include CRT display terminal 26 for displaying a graphical representation of a binding pocket of this invention using a program such as QUANTA as described herein. Output hardware might also include a printer 42, so that hard copy output may be produced, or a disk drive 24, to store system output for later use.

In operation, CPU 20 coordinates the use of the various input and output devices 36, 46, coordinates data accesses from mass storage 24 and accesses to and from working memory 22, and determines the sequence of data

processing steps. A number of programs may be used to process the machine-readable data of this invention. Such programs are discussed in reference to the computational methods of drug discovery as described herein. Specific references to components of the hardware system 10 are included as appropriate throughout the following description of the data storage medium.

Figure 3 shows a cross section of a magnetic data storage medium 100 which can be encoded with a machine-readable data that can be carried out by a system such as system 10 of Figure 2. Medium 100 can be a conventional floppy diskette or hard disk, having a suitable substrate 101, which may be conventional, and a suitable coating 102, which may be conventional, on one or both sides, containing magnetic domains (not visible) whose polarity or orientation can be altered magnetically. Medium 100 may also have an opening (not shown) for receiving the spindle of a disk drive or other data storage device 24.

The magnetic domains of coating 102 of medium 100 are polarized or oriented so as to encode in manner which may be conventional, machine readable data such as that described herein, for execution by a system such as system 10 of Figure 2.

Figure 4 shows a cross section of an optically-readable data storage medium 110 which also can be encoded with such a machine-readable data, or set of instructions, which can be carried out by a system such as system 10 of Figure 2. Medium 110 can be a conventional compact disk read only memory (CD-ROM) or a rewritable medium such as a magneto-optical disk which is optically readable and magneto-optically writable. Medium 100 preferably has a suitable substrate 111, which may be conventional, and a suitable coating 112, which may be conventional, usually of one side of substrate 111.

In the case of CD-ROM, as is well known, coating 112 is reflective and is impressed with a plurality of pits 113 to encode the machine-readable data. The arrangement of pits is read by reflecting laser light off the surface of coating 112. A protective coating 114, which preferably is substantially transparent, is provided on top of coating 112.

In the case of a magneto-optical disk, as is well known, coating 112 has no pits 113, but has a plurality of magnetic domains whose polarity or orientation can be changed magnetically when heated above a certain temperature, as by a laser (not shown). The

orientation of the domains can be read by measuring the polarization of laser light reflected from coating 112. The arrangement of the domains encodes the data as described above.

Thus, in accordance with the present invention, X-ray coordinate data capable of being processed into a three dimensional graphical display of a molecule or molecular complex which comprises a NS3 helicase-like binding pocket is stored in a machine-readable storage medium.

The NS3 helicase X-ray coordinate data, when used in conjunction with a computer programmed with software to translate those coordinates into the 3-dimensional structure of a molecule or molecular complex comprising a NS3 helicase-like binding pocket may be used for a variety of purposes, such as drug discovery.

For example, the structure encoded by the data may be computationally evaluated for its ability to associate with chemical entities. Chemical entities that associate with NS3 helicase may inhibit that enzyme, and are potential drug candidates. Alternatively, the structure encoded by the data may be displayed in a graphical three-dimensional representation on a computer screen. This allows visual inspection of the structure,

as well as visual inspection of the structure's association with chemical entities.

Thus, according to another embodiment, the invention relates to a method for evaluating the potential of a chemical entity to associate with

a) a molecule or molecular complex comprising a binding pocket defined by structure coordinates of NS3 helicase amino acids Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501 and Tyr502 according to Figure 1, or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

This method comprises the steps of:

i) employing computational means to perform a fitting operation between the chemical entity and a binding pocket of the molecule or molecular complex; and

ii) analyzing the results of said fitting operation to quantify the association between the chemical entity and the binding pocket.

The term "chemical entity", as used herein, refers to chemical compounds, complexes of at least two chemical compounds, and fragments of such compounds or

complexes.

Preferably, the method evaluates the potential of a chemical entity to associate with

a) a molecule or molecular complex comprising a binding pocket defined by structure coordinates of NS3 helicase amino acids Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501, Tyr502, Pro230, Val256, Thr298, Ala497, Lys551, Gln552, Gly554, Glu555, Asn556 and Pro558 according to Figure 1, or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

These embodiments relate to evaluating the potential of a chemical entity to associate with a NS3 helicase U8-like binding pocket.

In an alternate embodiment, the same steps indicated above are used in a method for evaluating the potential of a chemical entity to associate with

a) a molecule or molecular complex comprising a binding pocket defined by structure coordinates of NS3 helicase amino acids His369, Ser370, Lys371, Tyr392, Arg393, Thr411, Asp412, Ala413, Cys431, Val432,

Gln434, Ile446, Thr448, Arg461, Glu493, Glu555, Asn556 and Phe557 according to Figure 1, or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

These embodiments relate to evaluating the potential of a chemical entity to associate with a NS3 helicase U4-like binding pocket.

In yet another alternate embodiment, the same steps indicated above are used in a method for evaluating the potential of a chemical entity to associate with

a) a molecule or molecular complex comprising a binding pocket defined by structure coordinates of NS3 helicase amino acids Pro205, Thr206, Gly207, Ser208, Gly209, Lys210, Ser211, Thr212, Lys213, Asn229, Ala234, Gly237, Phe238, Tyr241, Asp290, Glu291, His293, Thr322, Ala323, Thr324, Gln460, Gly463, Arg464 and Arg467 according to Figure 1, or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the

backbone atoms of said amino acids of not more than 1.5Å.

These embodiments relate to evaluating the potential of a chemical entity to associate with a NS3 helicase NTP-like binding pocket.

Even more preferably, the method evaluates the potential of a chemical entity to associate with a molecule or molecular complex defined by structure coordinates of all of the NS3 helicase amino acids, as set forth in Figure 1, or a homologue of said molecule or molecular complex having a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

Alternatively, the structural coordinates of the NS3 helicase binding pocket can be utilized in a method for identifying a potential agonist or antagonist of a molecule comprising a NS3 helicase-like binding pocket. This method comprises the steps of:

a. using the atomic coordinates of Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501 and Tyr502 according to Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, to generate a three-dimensional structure of molecule comprising a NS3 helicase-like binding pocket;

b. employing said three-dimensional structure to design or select said potential agonist or antagonist;

c. synthesizing said agonist or antagonist; and

d. contacting said agonist or antagonist with said molecule to determine the ability of said potential agonist or antagonist to interact with said molecule.

More preferred is when the atomic coordinates of Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501, Tyr502, Pro230, Val256, Thr298, Ala497, Lys551, Gln552, Gly554, Glu555, Asn556 and Pro558 according to Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, are used to generate a three-dimensional structure of molecule comprising a NS3 helicase-like binding pocket.

These methods are designed to identify agonists and antagonists that associate with an NS3 helicase U8-like binding pocket.

Alternatively, the atomic coordinates of the NS3 helicase U4 binding pocket -- His369, Ser370, Lys371, Tyr392, Arg393, Thr411, Asp412, Ala413, Cys431, Val432, Gln434, Ile446, Thr448, Arg461, Glu493, Glu555, Asn556 and Phe557 according to Figure 1 -- ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, may be used in step a), above, to generate a three-dimensional structure of molecule comprising a NS3 helicase-like binding pocket.

In another alternative embodiment, the atomic coordinates of the NS3 helicase NTP binding site -- Pro205, Thr206, Gly207, Ser208, Gly209, Lys210, Ser211,

Thr212, Lys213, Asn229, Ala234, Gly237, Phe238, Tyr241, Asp290, Glu291, His293, Thr322, Ala323, Thr324, Gln460, Gly463, Arg464 and Arg467 according to Figure 1 -- ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, may be used in step a), above, to generate a three-dimensional structure of molecule comprising a NS3 helicase-like binding pocket.

Most preferred is when the atomic coordinates of all the amino acids of NS3 helicase according to Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, are used to generate a three-dimensional structure of molecule comprising a NS3 helicase-like binding pocket.

For the first time, the present invention permits the use of molecular design techniques to identify, select and design chemical entities, including inhibitory compounds, capable of binding to NS3 helicase-like binding pockets - in particular, the oligonucleotide binding pocket of NS3 helicase.

Applicants' elucidation of the U4 and U8 binding pockets in the oligonucleotide binding site and an expanded elucidation of the NTP binding pocket on NS3 helicase provides the necessary information for designing new chemical entities and compounds that may interact with NS3 helicase-like binding pockets, in whole or in part.

Throughout this section, discussions about the ability of an entity to bind to, associate with or

inhibit a NS3 helicase-like binding pocket refers to features of the entity alone. Assays to determine if a compound binds to NS3 helicase are well known in the art and are exemplified below.

The design of compounds that bind to or inhibit NS3 helicase-like binding pockets according to this invention generally involves consideration of two factors. First, the entity must be capable of physically and structurally associating with parts or all of the NS3 helicase-like binding pockets. Non-covalent molecular interactions important in this association include hydrogen bonding, van der Waals interactions, hydrophobic interactions and electrostatic interactions.

Second, the entity must be able to assume a conformation that allows it to associate with the NS3 helicase-like binding pocket directly. Although certain portions of the entity will not directly participate in these associations, those portions of the entity may still influence the overall conformation of the molecule. This, in turn, may have a significant impact on potency. Such conformational requirements include the overall three-dimensional structure and orientation of the chemical entity in relation to all or a portion of the binding pocket, or the spacing between functional groups

of an entity comprising several chemical entities that directly interact with the NS3 helicase-like binding pocket or homologues thereof.

The potential inhibitory or binding effect of a chemical entity on a NS3 helicase-like binding pocket may be analyzed prior to its actual synthesis and testing by the use of computer modeling techniques. If the theoretical structure of the given entity suggests insufficient interaction and association between it and the NS3 helicase-like binding pocket, testing of the entity is obviated. However, if computer modeling indicates a strong interaction, the molecule may then be synthesized and tested for its ability to bind to a NS3 helicase-like binding pocket. This may be achieved by testing the ability of the molecule to inhibit NS3 helicase using the assays described in Example 5. In this manner, synthesis of inoperative compounds may be avoided.

A potential inhibitor of a NS3 helicase-like binding pocket may be computationally evaluated by means of a series of steps in which chemical entities or fragments are screened and selected for their ability to associate with the NS3 helicase-like binding pockets.

One skilled in the art may use one of several methods to screen chemical entities or fragments for their ability to associate with a NS3 helicase-like binding pocket. This process may begin by visual inspection of, for example, a NS3 helicase-like binding pocket on the computer screen based on the NS3 helicase structure coordinates in Figure 1 or other coordinates which define a similar shape generated from the machine-readable storage medium. Selected fragments or chemical entities may then be positioned in a variety of orientations, or docked, within that binding pocket as defined supra. Docking may be accomplished using software such as Quanta and Sybyl, followed by energy minimization and molecular dynamics with standard molecular mechanics force fields, such as CHARMM and AMBER.

Specialized computer programs may also assist in the process of selecting fragments or chemical entities. These include:

1. GRID (P. J. Goodford, "A Computational Procedure for Determining Energetically Favorable Binding Sites on Biologically Important Macromolecules", J. Med. Chem., 28, pp. 849-857 (1985)). GRID is available from Oxford University, Oxford, UK.

2. MCSS (A. Miranker et al., "Functionality Maps of Binding Sites: A Multiple Copy Simultaneous Search Method." Proteins: Structure, Function and Genetics, 11, pp. 29-34 (1991)). MCSS is available from Molecular Simulations, San Diego, CA.

3. AUTODOCK (D. S. Goodsell et al., "Automated Docking of Substrates to Proteins by Simulated Annealing", Proteins: Structure, Function, and Genetics, 8, pp. 195-202 (1990)). AUTODOCK is available from Scripps Research Institute, La Jolla, CA.

4. DOCK (I. D. Kuntz et al., "A Geometric Approach to Macromolecule-Ligand Interactions", J. Mol. Biol., 161, pp. 269-288 (1982)). DOCK is available from University of California, San Francisco, CA.

Once suitable chemical entities or fragments have been selected, they can be assembled into a single compound or complex. Assembly may be preceded by visual inspection of the relationship of the fragments to each other on the three-dimensional image displayed on a computer screen in relation to the structure coordinates of NS3 helicase. This would be followed by manual model

building using software such as Quanta or Sybyl [Tripos Associates, St. Louis, MO].

Useful programs to aid one of skill in the art in connecting the individual chemical entities or fragments include:

1. CAVEAT (P. A. Bartlett et al, "CAVEAT: A Program to Facilitate the Structure-Derived Design of Biologically Active Molecules", in Molecular Recognition in Chemical and Biological Problems", Special Pub., Royal Chem. Soc., 78, pp. 182-196 (1989); G. Lauri and P. A. Bartlett, "CAVEAT: a Program to Facilitate the Design of Organic Molecules", J. Comput. Aided Mol. Des. , 8, pp. 51-66 (1994)). CAVEAT is available from the University of California, Berkeley, CA.

2. 3D Database systems such as ISIS (MDL Information Systems, San Leandro, CA). This area is reviewed in Y. C. Martin, "3D Database Searching in Drug Design", J. Med. Chem., 35, pp. 2145-2154 (1992).

3. HOOK (M. B. Eisen et al, "HOOK: A Program for Finding Novel Molecular Architectures that Satisfy the Chemical and Steric Requirements of a Macromolecule Binding Site", Proteins: Struct., Funct., Genet., 19,

pp. 199-221 (1994). HOOK is available from Molecular Simulations, San Diego, CA.

Instead of proceeding to build an inhibitor of a NS3 helicase-like binding pocket in a step-wise fashion one fragment or chemical entity at a time as described above, inhibitory or other NS3 helicase binding compounds may be designed as a whole or "de novo" using either an empty binding site or optionally including some portion(s) of a known inhibitor(s). There are many de novo ligand design methods including:

1. LUDI (H.-J. Bohm, "The Computer Program LUDI: A New Method for the De Novo Design of Enzyme Inhibitors", J. Comp. Aid. Molec. Design, 6, pp. 61-78 (1992)). LUDI is available from Molecular Simulations Incorporated, San Diego, CA.

2. LEGEND (Y. Nishibata et al., Tetrahedron, 47, p. 8985 (1991)). LEGEND is available from Molecular Simulations Incorporated, San Diego, CA.

3. LeapFrog (available from Tripos Associates, St. Louis, MO).

4. SPROUT (V. Gillet et al, "SPROUT: A Program for Structure Generation)", J. Comput. Aided Mol. Design, 7,

pp. 127-153 (1993)). SPROUT is available from the University of Leeds, UK.

Other molecular modeling techniques may also be employed in accordance with this invention [see, e.g., N. C. Cohen et al., "Molecular Modeling Software and Methods for Medicinal Chemistry, J. Med. Chem., 33, pp. 883-894 (1990); see also, M. A. Navia and M. A. Murcko, "The Use of Structural Information in Drug Design", Current Opinions in Structural Biology, 2, pp. 202-210 (1992); L. M. Balbes et al., "A Perspective of Modern Methods in Computer-Aided Drug Design", in Reviews in Computational Chemistry, Vol. 5, K. B. Lipkowitz and D. B. Boyd, Eds., VCH, New York, pp. 337-380 (1994); see also, W. C. Guida, "Software For Structure-Based Drug Design", Curr. Opin. Struct. Biology,, 4, pp. 777-781 (1994)].

Once a compound has been designed or selected by the above methods, the efficiency with which that entity may bind to an NS3 helicase binding pocket may be tested and optimized by computational evaluation. For example, an effective NS3 helicase binding pocket inhibitor must preferably demonstrate a relatively small difference in energy between its bound and free states (i.e., a small deformation energy of binding). Thus, the

most efficient NS3 helicase binding pocket inhibitors should preferably be designed with a deformation energy of binding of not greater than about 10 kcal/mole, more preferably, not greater than 7 kcal/mole. NS3 helicase binding pocket inhibitors may interact with the binding pocket in more than one conformation that is similar in overall binding energy. In those cases, the deformation energy of binding is taken to be the difference between the energy of the free entity and the average energy of the conformations observed when the inhibitor binds to the protein.

An entity designed or selected as binding to an NS3 helicase binding pocket may be further computationally optimized so that in its bound state it would preferably lack repulsive electrostatic interaction with the target enzyme and with the surrounding water molecules. Such non-complementary electrostatic interactions include repulsive charge-charge, dipole-dipole and charge-dipole interactions.

Specific computer software is available in the art to evaluate compound deformation energy and electrostatic interactions. Examples of programs designed for such uses include: Gaussian 94, revision C (M. J. Frisch, Gaussian, Inc., Pittsburgh, PA ©1995);

AMBER, version 4.1 (P. A. Kollman, University of California at San Francisco, ©1995); QUANTA/CHARMM (Molecular Simulations, Inc., San Diego, CA ©1995); Insight II/Discover (Molecular Simulations, Inc., San Diego, CA ©1995); DelPhi (Molecular Simulations, Inc., San Diego, CA ©1995); and AMSOL (Quantum Chemistry Program Exchange, Indiana University). These programs may be implemented, for instance, using a Silicon Graphics workstation such as an Indigo^2 with "IMPACT" graphics. Other hardware systems and software packages will be known to those skilled in the art.

Another approach enabled by this invention, is the computational screening of small molecule databases for chemical entities or compounds that can bind in whole, or in part, to a NS3 helicase binding pocket. In this screening, the quality of fit of such entities to the binding site may be judged either by shape complementarity or by estimated interaction energy [E. C. Meng et al., J. Comp. Chem., 13, pp. 505-524 (1992)].

According to another embodiment, the invention provides compounds which associate with a NS3 helicase-like binding pocket produced or identified by the method set forth above.

The structure coordinates set forth in Figure 1 can also be used to aid in obtaining structural information about another crystallized molecule or molecular complex. This may be achieved by any of a number of well-known techniques, including molecular replacement.

Therefore, in another embodiment this invention provides a method of utilizing molecular replacement to obtain structural information about a molecule or molecular complex whose structure is unknown comprising the steps of:

a) crystallizing said molecule or molecular complex of unknown structure;

b) generating X-ray diffraction data from said crystallized molecule or molecular complex; and

c) applying at least a portion of the structure coordinates set forth in Figure 1 to the X-ray diffraction data to generate a three-dimensional electron density map of the molecule or molecular complex whose structure is unknown.

By using molecular replacement, all or part of the structure coordinates of the NS3 helicase/ oligonucleotide complex as provided by this invention (and set forth in Figure 1) can be used to determine the

structure of a crystallized molecule or molecular complex whose structure is unknown more quickly and efficiently than attempting to determine such information ab initio.

Molecular replacement provides an accurate estimation of the phases for an unknown structure. Phases are a factor in equations used to solve crystal structures that can not be determined directly. Obtaining accurate values for the phases, by methods other than molecular replacement, is a time-consuming process that involves iterative cycles of approximations and refinements and greatly hinders the solution of crystal structures. However, when the crystal structure of a protein containing at least a homologous portion has been solved, the phases from the known structure provide a satisfactory estimate of the phases for the unknown structure.

Thus, this method involves generating a preliminary model of a molecule or molecular complex whose structure coordinates are unknown, by orienting and positioning the relevant portion of the NS3 helicase/oligonucleotide complex according to Figure 1 within the unit cell of the crystal of the unknown molecule or molecular complex so as best to account for the observed X-ray diffraction data of the crystal of the

molecule or molecular complex whose structure is unknown. Phases can then be calculated from this model and combined with the observed X-ray diffraction data amplitudes to generate an electron density map of the structure whose coordinates are unknown. This, in turn, can be subjected to any well-known model building and structure refinement techniques to provide a final, accurate structure of the unknown crystallized molecule or molecular complex [E. Lattman, "Use of the Rotation and Translation Functions", in Meth. Enzymol., 115, pp. 55-77 (1985); M. G. Rossmann, ed., "The Molecular Replacement Method", Int. Sci. Rev. Ser., No. 13, Gordon & Breach, New York (1972)].

The structure of any portion of any crystallized molecule or molecular complex that is sufficiently homologous to any portion of the NS3 helicase/oligonucleotide complex can be resolved by this method.

In a preferred embodiment, the method of molecular replacement is utilized to obtain structural information about another helicase. The structure coordinates of NS3 helicase as provided by this invention are particularly useful in solving the structure of other

isoforms of NS3 helicase or other NS3 helicase-containing complexes.

Furthermore, the structure coordinates of NS3 helicase as provided by this invention are useful in solving the structure of NS3 helicase proteins that have amino acid substitutions, additions and/or deletions (referred to collectively as "NS3 helicase mutants", as compared to naturally occurring NS3 helicase isoforms. These NS3 helicase mutants may optionally be crystallized in co-complex with a chemical entity, such as a non-hydrolyzable NTP analogue or an oligonucleotide. The crystal structures of a series of such complexes may then be solved by molecular replacement and compared with that of wild-type NS3 helicase. Potential sites for modification within the various binding sites of the enzyme may thus be identified. This information provides an additional tool for determining the most efficient binding interactions, for example, increased hydrophobic interactions, between NS3 helicase and a chemical entity or compound.

The structure coordinates are also particularly useful to solve the structure of crystals of NS3 helicase or NS3 helicase homologues co-complexed with a variety of chemical entities. This approach enables the

determination of the optimal sites for interaction between chemical entities, including between candidate NS3 helicase inhibitors and NS3 helicase. For example, high resolution X-ray diffraction data collected from crystals exposed to different types of solvent allows the determination of where each type of solvent molecule resides. Small molecules that bind tightly to those sites can then be designed and synthesized and tested for their NS3 helicase inhibition activity.

All of the complexes referred to above may be studied using well-known X-ray diffraction techniques and may be refined versus 1.5-3 Δ resolution X-ray data to an R value of about 0.20 or less using computer software, such as X-PLOR [Yale University, ©1992, distributed by Molecular Simulations, Inc.; see, e.g., Blundell & Johnson, supra; Meth. Enzymol., vol. 114 & 115, H. W. Wyckoff et al., eds., Academic Press (1985)]. This information may thus be used to optimize known NS3 helicase inhibitors, and more importantly, to design new NS3 helicase inhibitors.

In order that this invention be more fully understood, the following examples are set forth. These examples are for the purpose of illustration only and are

not to be construed as limiting the scope of the invention in any way.

EXAMPLE 1

Cloning and Expression of NS3 Helicase

The HCV NS3 RNA helicase domain (encoded by nucleotides 502-1896 of SEQ ID NO:6) was subcloned from a cDNA of the HCV H strain [A. Grakoui et al., J. Virol., 67, pp. 1385-95 (1993); C. Lin et al., J. Virol., 68, pp. 8147-57 (1994), the disclosures of which are herein incorporated be reference] into a pET expression vector (Novagen, Madison, WI). The resulting plasmid, pET-BS(+)/HCV/NS3-C465-His (SEQ ID NO:4), also contained a methionine start codon, a linker encoded Gly-Ser-Gly-Ser sequence attached the C-terminal threonine of the NS3 helicase domain and a six-histidine tag fused to the C-terminus of the Gly-Ser-Gly-Ser sequence to facilitate protein purification. This plasmid was used as a template for single-stranded DNA-based site-directed mutagenesis essentially as described by (T.A. Kunkel, Proc. Natl. Acad. Sci. USA, 82, pp.488-492 (1985) and C. Lin et al., Virology, 192, pp.596-604 (1993), the disclosures of which are herein incorporated by reference) with the following modifications.

The single stranded phagemid DNA packaged in the presence of helper M13 phage corresponds to the HCV plus strand. A single colony of *E. coli* strain CJ 326, transformed with pET-BS(+)/HCV/NS3-C465-His, was grown in YT media containing 0.25 µg/ml of uridine and 50 µg/ml of carbenicillin. After three serial passages, M13 helper phage (Bio-Rad) was used to rescue uridylated phagemid single stranded DNA, which was then used as template for oligonucleotide-directed mutagenesis [T.A. Kunkel (1985), supra]. ABI automatic sequencing was used to identify mutations and ensure that there is no other unintended mutation within the HCV NS3 helicase domain sequences. Construct containing mutations were named according to the position of the substituted residue in the full-length HCV NS3 protein.

In this manner, we made NS3 helicase corresponding to the consensus sequence of the HCV genotype 1 (Pro at amino acid 332; Ser at amino acid 403; Ala at amino acid 410; and Thr at amino acid 505; hereinafter referred to as "wild type"); as well as NS3 helicase containing the following single amino acid mutations as compared to the consensus HCV genotype 1 NS3 helicase sequence: Ser231-to-Ala; Thr269-to-Ala; Ser370-to-Ala; Thr411-to-Ala; Trp501-to-Phe; Trp501-to-Leu; and

Trp501-to-Ala.

E. coli BL21(DE3) cells, freshly transformed with the pET-BS(+)/HCV/NS3-C465-His plasmid or similar plasmids encoding the single amino acid mutant NS3 helicases described above, were grown at 30°C in LB media supplemented with 50 µg/ml of carbenicillin. When the density reached an OD_{600} of 1.0, the cells were induced for 3 hr at 30°C by the addition of IPTG to a final concentration of 0.8 mM. After induction, the cells were harvested and stored frozen at -70°C until purification.

All the protein purification procedures were performed at 4°C. Typically, 10 g of cell paste was resuspended in 50 ml of buffer A [50 mM HEPES (pH 8), 300 mM NaCl, 10 % glycerol, and 2.5 mM β-mercaptoethanol] containing 0.2 mM phenylmethylsulfonyl fluoride (PMSF), and lysed using a microfluidizer. The lysate was clarified by centrifugation at 100,000 x g for 35 min. We then added 5 mM imidazole (pH 8) to the supernatant and the resulting solution was incubated for 2 hours with 2 ml of Ni-NTA-agarose (Qiagen, Chatsworth, CA).

The resin was packed into a column and washed with 10 bed volumes of buffer A containing 5 mM and 15 mM imidazole, and eluted with buffer A containing 100 mM imidazole. The eluant was desalted to buffer B [50 mM

HEPES (pH 8), 10 % glycerol, and 2.5 mM β-mercaptoethanol] containing 50 mM NaCl on a PD-10 column (Pharmacia). The desalted solution was loaded onto a Heparin-Sepharose column (Pharmacia). The flow-through was then applied onto a Q-Sepharose column (Pharmacia) and washed with 10 bed volumes of buffer B containing 50 mM NaCl. The column was then eluted with a NaCl gradient from 50 mM to 2M in buffer B.

The peak fraction containing the HCV NS3 helicase domain protein was shown by gel-filtration chromatography to be monomeric. The purified protein was judged to be greater than 90% pure by sodium dodecyl sulfate (SDS) polyacrylamide gel electrophoresis (PAGE) and Coomassie R-250 staining.

For crystallization studies, the protein was concentrated to 10 mg/ml by ultrafiltration and slowly diluted with 5 volumes of 15 mM MES (pH 6.5), 2.5 mM β-mercaptoethanol and again concentrated to 10 mg/ml. The dilution step was then repeated with 2 volumes of the MES buffer and concentrated to 13 mg/ml. We then added oligonucleotide (dU_6; Oligo Therapeutics, Inc., Wilsonville, OR) to yield a 1:1 molar ration of protein to nucleic acid.

To produce recombinant full-length NS3 protein which was subsequently used for mutagenesis studies in the NTP binding pocket, we followed similar procedures as above. The full length NS3 coding sequence was also subcloned from the HCV H strain. It was placed in a pET expression vector to create the plasmid pET-BS(+)/HCV/FLNS3-His (SEQ ID NO:3). As with the helicase constructs previously described, the full-length NS3 coding sequence was preceded by a methionine start codon and had codons encoding Gly-Ser-Gly-Ser-His_6 in frame at the C-terminus of the NS3 coding region. That plasmid was used as a template for single-stranded DNA-based site-directed mutagenesis as described above.

In this manner, we made NS3 containing the following single amino acid mutations as compared to the consensus HCV genotype 1 NS3 helicase sequence: Gln460->Ala, Arg461->Ala, Arg462->Ala, Arg464->Ala and Arg467->Ala.

Both the wild-type full-length NS3 and the single amino acid mutants were purified as described above.

EXAMPLE 2

Crystallization and Data Collection

Crystals of the NS3 helicase:dU_8 complex were grown by hanging-drop vapor diffusion over wells containing 0.1 M Tris pH 8.0, 0.2 M Li_2SO_4, 18% Polyethylene glycol 6000, and 8 mM β-mercaptoethanol. Drops were macroseeded within 12 hours after being set up. Crystals grew over the course of 2-3 weeks to dimensions of 0.4 x 0.4 x 0.1 mm^3. The crystals belong to space group $P2_12_12$ with unit cell dimensions a=73.1Å b=117.5Å, c=63.4Å, and contain one helicase:dU_8 complex per asymmetric unit.

Heavy atom soaks were carried out by transferring crystals to a solution containing 0.1 M Tris pH 8.0, 0.2 M Li_2SO_4, 17% Polyethylene glycol 6000, 8 mM β-mercaptoethanol, in addition to the heavy atom in question. Heavy atom soaks with K_2WO_4 were performed in the absence of Li_2SO_4.

Crystals were transferred to a solution containing 0.08 M Tris pH 8.0, 0.2 M Li_2SO_4, 16% Polyethylene glycol 6000, 8 mM β-mercaptoethanol, and 15% glycerol and immediately frozen in a dry nitrogen gas stream at 100 K (Molecular Structure Corp., Houston, TX) for data collection.

Data was acquired by oscillation photography on a Rigaku R-AXIS IIC phosphor imaging area detector

mounted on a Rigaku RU200 rotating anode generator (MSC), operating at 50kV and 100mA. Measured intensities were integrated, scaled, and merged using the HKL software package [Z. Otwinowski et al., Meth. Enzymol., 276, pp. 307-326 (1997)].

EXAMPLE 3

Phasing, model building and refinement

Heavy atom positions were located from difference Patterson and anomalous difference Patterson maps and confirmed with difference Fourier syntheses. Heavy atom parameters were refined and phases computed to 2.3Å using the program PHASES [W. Furey et al., Meth. Enzymol., 277, pp. 590-620, (1997) need full cite]. MIR phases were improved by cycles of solvent flattening [B. C. Wang,. Methods Enzymol., 115, pp. 90-112 (1985)] combined with histogram matching [K. Y. J. Zhang et al., Acta Crystallogr., A46, pp.377-381 (1990)] using the CCP4 crystallographic package [CCP4; C. C. Project, Acta Crystallogr., D50, pp. 760-763 (1994)].

Model building was carried out using QUANTA96 (Molecular Simulations), and all refinement done in XPLOR [A. T. Brunger, "X-PLOR: A System for X-Ray Crystallography and NMR," Yale University Press, New

Haven, Connecticut. (1993)], using the free R-value [A. T. Brunger, Nature, 355, pp. 472-475 (1992)] to monitor the course of refinement. The current model, refined using data from 6.0-2.2Å, consists of NS3 helicase residues 190-414 and 418-626, residues 3-8 of dU_8, 1 bound sulfate ion, and 159 well-ordered water molecules.

EXAMPLE 4

Structural Features of the NS3 Helicase-dU_8 Complex

The structure of the resolved portion of HCV NS3 helicase (NS3 residues 189-626 of SEQ ID NO:1, corresponding to HCV polyprotein residues 1215-1652) complexed with a deoxyuridine octamer (dU_8) was determined by multiple isomorphous replacement combined with anomalous scattering. The protein consists of three domains separated by a series of clefts (Figure 5).

Domains 1 and 3 share a more extensive interface than either share with domain 2. This interface is largely accounted for by packing of helices $\alpha5$ and $\alpha6$ from domain 3 on helix $\alpha4$ from domain 1. As a result, the clefts between domains 1 and 2 and domains 2 and 3 are the largest. A published crystal structure of HCV NS3 helicase domain demonstrated that domain 2 could undergo rigid body movements relative to domains 1 and 3

based on a comparison of two crystallographically independent molecules [N. Yao et al., Nat. Struct. Biol., 4, pp. 463-467 (1997)]. Preliminary structural studies on HCV helicase in a different crystal form also show a rotation of domain 2 relative to the first and third, confirming that this domain is flexibly linked to the other two.

Domains 1 and 2 of the HCV helicase, which contain all of the conserved helicase sequence motifs, have similar topologies (Figure 6) and are also similar to domains 1A and 2A of the four domain PcrA and Rep DNA helicases [H. S. Subramanya et al., Nature, 384, pp. 379-383 (1996); S. Korolev et al., Cell, 90, pp. 635-647 (1997)]. The structurally homologous domains of PcrA, Rep, and HCV helicases each contain a parallel six-stranded ß-sheet flanked by α-helices. In addition, domain 1 of HCV helicase contains a seventh ß-strand running antiparallel to the rest of the sheet.

Superposition of domains 1 and 2 yields an rms deviation of 2.0 Å for 76 C-alpha atoms that form the core of each domain. Domain 3 is predominantly α-helical and is associated with domain 2 by a pair of anti-parallel ß-strands (Figure 5). An interesting component of domain 3 is a 40 amino acid region preceding the C-

terminal α-helix that lacks secondary structure elements. This may represent a flexible region of the protein that allows the C-terminus of NS3 to reach the active site of its own serine protease domain to facilitate cleavage at the NS3/NS4A junction during HCV polyprotein processing. This cleavage is believed to occur in cis [R. Bartenschlager et al., J. Virol., 68, pp. 5045-5055 (1994)].

The N-terminal region of domain 1 contains a phosphate binding loop that is highly conserved among all helicases and commonly referred to as the Walker A box or motif I [J. E. Walker et al., EMBO J., 1, pp. 945-951 (1982)]. In the structure presented here, this loop contains a bound sulfate ion (Figure 7A). This phosphate binding loop is structurally similar to those found in a number of other ATPases [M. Saraste et al., Trends Biochem. Sci., 15, 430-434 (1990)]. The sulfate ion is stabilized by hydrogen bonds from the amide nitrogens of Gly-207 and Gly-209, and the side chains of Ser-208, Lys-210, and Ser-211. Lys-210 makes an additional water-mediated contact to the conserved Asp-290 of the DECH motif (motif II or Walker motif B).

The side chains of Asp-290 and Glu-291, the most conserved residues in the DECH motif, point toward

an open area beneath the phosphate binding loop that presumably is occupied by Mg^{2+} and the γ-phosphate of the bound Mg^{2+}-NTP substrate. Cys-292 is buried in the protein interior while the His-293 side chain points into the cleft between domains 1 and 2. The position of the sulfate in this structure appears to be very similar to that of the ß-phosphate of ADP in the PcrA helicase:ADP complex [H. S. Subramanya et al., Nature, (1996), supra]. It is therefore likely that this sulfate ion occupies the position of the ß-phosphate when NTP or NDP is bound to the HCV helicase.

Highly conserved residues Gln-460, Arg-464, and Arg-467 from domain 2 are solvent exposed in the interdomain cleft, while Arg-461 and Arg-462 are buried in domain 2 and stabilized by internal salt bridges and hydrogen bonds. The position of Arg-461 contrasts that described in the structure of the apo HCV NS3 helicase, which reported this side chain as being solvent exposed and interacting with the phosphate backbone of single stranded nucleic acid modeled into this cleft [N. Yao et al., Nat. Struct. Biol., (1997), supra].

Protein-single stranded DNA interactions

Studies of HCV NS3 helicase single stranded nucleic acid binding have demonstrated that poly(dU) binds to the helicase with higher affinity than poly(rU) of the same length [F. Preugschat et al, J. Biol. Chem., 271 (1996), supra]. Extrapolation of this data suggested that a deoxyoligonucleotide 8mer might be long enough to bind to the helicase with high affinity and not interfere with protein-protein contacts during crystallization. Therefore an oligo dU_8 was used for complex crystallization. In the structure presented here the first two residues of the oligonucleotide are disordered and have not been included in the model. The sugar-phosphate backbone of the third nucleotide is well represented in electron density maps (Figure 7B) while density for the base is extremely weak. Electron density for residues 4-8 is very well defined for the sugar-phosphate backbone and slightly weaker for the bases. Preliminary studies with dU_{10} and dU_{12} oligonucleotides show essentially the same electron density for the DNA.

The bound single stranded DNA ("ssDNA") lies in a channel approximately 16 angstroms in diameter that separates domain 3 from domains 1 and 2 (Figure 10). The 5' end of the oligonucleotide resides at the interface of domains 2 and 3 and its 3' end at the interface of

domains 1 and 3. This orientation of the DNA is roughly perpendicular to that of the ssRNA in a model derived from the apo HCV helicase structure, in which the ssRNA was placed in the cleft between domains 1 and 2 [N. Yao et al., Nat. Struct. Biol., (1997), supra]. It is, however, consistent with the oligonucleotide binding site in the Rep helicase:DNA structure [S. Korolev et al., Cell, (1997), supra].

Interactions between the ssDNA and enzyme are mostly confined to the DNA backbone, as would be expected for a nonspecific protein-nucleic acid complex, and are concentrated at the two ends of the oligonucleotide. Protein contacts emanate mostly from loops between secondary structural elements in domains 1 and 2 (Figures 6A,B). Interestingly, these contacts arise from symmetrically equivalent residues in these two domains, so that protein contacts to the dU4 and dU5 backbone phosphates are nearly identical to those to the dU7 and dU8 phosphates.

At the 3' end of the DNA the dU8 phosphate is stabilized by a hydrogen bond with Thr-269 Oγ, which in turn accepts a hydrogen bond from the main chain NH of Lys-272, and by a hydrogen bond to the main chain NH of Gly-255. Equivalent contacts to the dU5 phosphate are

made by the Arg-393 main chain NH and Thr-411 Oγ, which accepts a hydrogen bond from the Ala-413 NH. The dU7 phosphate accepts a hydrogen bond from the Val-232 NH and interacts with the Ala-233 NH and Ser-231 Oγ via a bridging water molecule. The direct and water mediated main chain interactions are duplicated by Lys-371 and Lys-372 from domain 2 to the dU4 phosphate. Ser-370, the equivalent residue in domain 2 to Ser-231, makes a water mediated contact to the dU3 phosphate rather than dU4. Superposition of domains 1 and 2 of HCV helicase reveals that the residues involved in phosphate contacts are structurally equivalent (Figure 6). This was an unanticipated finding based on the poor sequence homology between these two domains. Additionally, the four residues interacting with the phosphate backbone, Ser-231, Thr-269, Ser-370, and Thr-411, are absolutely conserved in all HCV NS3 sequences known to date. These findings suggest that these two domains may have arisen from a gene duplication event.

Residues dU4-dU8 are capped by interactions at each end with hydrophobic side chains. Trp-501 stacks with the base of dU8 while Val-432 interacts with the dU4 base (Figure 10). These two side chains act as a pair of bookends, defining a central binding cavity occupied by

five nucleotides. Both Val-432 and Trp-501 are highly conserved among HCV NS3 sequences but neither have been implicated in nucleic acid binding nor duplex unwinding. The Val-432:dU4 base interaction induces significant rotation about the phosphate backbone between dU3 and dU4 such that the bases are completely unstacked (Figure 10). Stacking of Trp-501 with the dU8 base should similarly necessitate a large rotation about the phosphate of the following nucleotide. The resulting conformation of the DNA could be stabilized by phosphate interactions with Arg-253 and Lys-272 from domain 1 and Lys-372 and Lys-373 from domain 2, which lie outside the central binding cavity.

Domain 2 contains a pair of extended anti-parallel strands encompassing residues 430-452, which are involved in binding the 5' end of the oligonucleotide (Figure 5). Two other single-strand polynucleotide binding proteins, SSB and tRNA synthetase, contain anti-parallel strands extending from their protein core that are thought to make up the nucleic acid binding site [S. Raghunathan et al., Proc. Natl. Acad. Sci. USA, 94, pp. 6652-6657 (1997); M. Ruff et al., Science, 252, pp. 1682-1689 (1991)]. This region is termed the L45 loop in this class of nucleic acid binding proteins. In the HCV

helicase structure the oligonucleotide binds in a channel spanning two protein domains in a manner roughly similar to that seen for replication protein A (RPA) [A. Bochkarev et al., Nature, 385, pp. 176-181 (1997)]. In both structures, the oligonucleotide is most tightly bound at the 3' and 5' ends with few contacts with the central nucleotides. RPA also contains an L45 loop, which binds to the 5' end of the oligonucleotide.

The five residues occupying the central binding cavity of HCV helicase adopt a conformation reminiscent of the central base pairs of DNA in the TBP-TATA box complex structures [Y. Kim et al., Nature, 365, pp. 512-520 (1993); J. L. Kim et al., Nature, 365, pp. 520-527 (1993)]. In both instances the DNA is underwound considerably and the backbone smoothly bent, compressing the edges of the bases. Comparison of the DNA structure here with the central pyrimidine stretch of the TATA box DNA reveals that this DNA is more underwound than that seen in the TBP-TATA box complex.

Our structure of the helicase:dU_8 complex does not offer a ready explanation as to why the enzyme binds to poly(dU) with higher affinity than to other homopolymer DNAs [F. Preugschat et al, J. Biol. Chem., 271 (1996), supra]. Sequence specific interactions with

the DNA bases are not observed within the central binding cavity of the helicase. Differences in DNA binding affinity between different sequences in this case may be a result of differences in energetics of DNA distortion and base stacking rather than base-specific hydrogen bonding patterns.

Location of conserved sequence motifs

There is very high sequence conservation among various HCV strains in the NS3 RNA helicase domain with >80% sequence identity over the entire 456 amino acid polypeptide. The most highly conserved segments of these domains correspond to the canonical helicase sequence motifs (Figures 8, 9A) [A. Gorbalenya et al., Curr. Opin. Struct. Biol., 3, pp. 419-429 (1993)]. In the three-dimensional structure residues from these motifs form the interface between the first two domains (Figure 9B). Visual inspection of the structures of the PcrA DNA helicase from *Bacillus stearothermophilus* [H. S. Subramanya et al., Nature, (1996), supra] and *E. coli* Rep DNA helicase [S. Korolev et al., Cell (1997), supra; coordinates not available] suggests overall structural similarity between domains 1A and 2A of these DNA helicases and domains 1 and 2 of the HCV helicase. The

locations of the conserved DNA helicase sequence motifs overlap with those of the HCV helicase allowing an unambiguous alignment of these motifs. Mutagenesis of individual residues within these motifs in HCV helicase or in other RNA helicases have demonstrated that they are essential for enzyme activity. The individual phenotypes of these mutants can now be more fully explained using the enzyme structure.

Domain 1 of the HCV helicase has a fold similar to that found in a number of adenosine triphosphate transphosphorylases, such as adenylate and thymidine kinases. In particular, the phosphate binding loop formed by motif I (GSGKT) is virtually identical to the corresponding loop in the kinases. In these kinases this loop is involved in binding the ß phosphate of ATP. HCV helicase has a sulfate bound in this exact location (Figure 7A). Mutation of residues corresponding to HCV helicase Lys-210 in other helicases invariably leads to inactivation [J. W. George et al., J. Mol. Biol., 235, 424-435 (1994); T. W. Seeley et al., J. Biol. Chem., 265, pp. 7158-7165 (1990)].

Motif II (DExH) is proximal to the GSGKT phosphate binding loop and is expected to be involved in binding the Mg^{2+}-ATP substrate. In adenylate and

thymidine kinases, a conserved aspartate binds Mg^{2+}, which helps orient the ATP for nucleophilic attack [M. E. Black et al., J. Biol. Chem., 267, pp. 6801-6806 (1992); H. G. Yan et al., Biochemistry, 30, pp. 5539-5546 (1991)]. Mutation of the equivalent aspartate residue in these kinases or in other helicases inactivates ATP hydrolysis [M. E. Black et al., J. Biol. Chem., (1992), supra; C. H. Gross et al., J. Virol., 69, pp. 4727-4736 (1995); R. M. Brosh Jr., et al., J. Bacteriol., 177, pp. 5612-562 (1995); A. Pause et al., EMBO J., 11, pp. 2643-2654 (1992)]. His-293 is located at the bottom of the interdomain cleft and approximately 4 Å away from Val-456 and Gln-460. This histidine appears to be essential for coupling the ATPase activity to polynucleotide binding; mutations of this histidine in HCV NS3 and vaccinia NPH-II helicases result in a functional ATPase with no helicase activity [C. H. Gross et al., J. Virol., (1995), supra; G. M. Heilek et al. J. Virol., 71, 6264-6266 (1997)]. Unfortunately, the structure presented here does not provide an obvious explanation as to how this residue couples the NTPase and unwinding activities.

Studies in several helicases have looked at the effects of mutations in motif VI (QRxGRxGR), yet a role for this motif has not been clearly defined. In the HCV

helicase residues in this motif are located in the 1:2 interdomain cleft. Gln-460 lies at the bottom of the cleft opposite from His-293. Mutation of the corresponding glutamine in vaccinia virus helicase and in eIF-4A leads to significant decreases in ATPase activity [A. Pause et al., EMBO J., (1992), supra; C. H. Gross et al., J. Virol., 70, pp. 1706-1713 (1996)]. There are three conserved arginines in motif VI that were proposed by N. Yao et al., Nat. Struct. Biol. (1997), supra, to be involved in binding single-stranded RNA in the cleft between domains 1 and 2. Our structure of the helicase:dU_8 complex demonstrates that this interpretation is unlikely to be correct.

Here Arg-461 points away from the cleft and is hydrogen-bonded to Asp-412 and Asp-427. Mutation of this residue in a vaccinia virus helicase leads to decreases in RNA binding [C. H. Gross et al., J. Virol., (1996), supra], possibly as a consequence of alterations in the conformation of Asp-412 which lines the polynucleotide binding channel. Arginines 464 and 467 extend into the interdomain cleft, directly across from the presumed locations of the γ and α phosphates of ATP. These residues appear to be poised to contact the ATP phosphates upon closure of this interdomain cleft. This

would be similar to the function of conserved basic residues in the second domain of adenylate kinase.

Consistent with the possibility that Arg-464 and Arg-467 are directly involved in ATP binding, mutations of the corresponding residues to Ala or Gln in vaccinia NPH-II or eIF-4A reduce the ATPase activity to <20% of wild type levels [C. H. Gross et al., J. Virol., (1996), supra; A. Pause et al., Mol. Cell. Biol., 13, pp. 6789-6798 (1993)]. Arg-467 appears to be conserved among all three helicase superfamilies (Figure 9A) [A. Gorbalenya et al., Curr. Opin. Struct. Biol. (1993), supra]

Motif III connects domains 1 and 2, and appears to be a flexible linker [N. Yao et al., Nat. Struct. Biol. (1997), supra]. Motif Ia forms part of the ß sheet core of domain 1, but also extends to the oligonucleotide. Residues in motif V both contact the oligonucleotide and line the interface between the first two domains. In particular, Thr-411 makes a hydrogen bond to the phosphate of dU3 of the oligonucleotide.

The current structure lacks any region corresponding to motif IV in Rep and PcrA helicases [H. S. Subramanya et al., Nature (1996), supra; S. Korolev et al., Cell, (1997), supra], members of the superfamily I

class of helicases. Previous sequence alignments that found similarities within motif IV between superfamily I and II helicases were done with rather weak criteria and may not have been significant. In the DNA helicases, motif IV is responsible for binding the adenine ring of ATP [H. S. Subramanya et al., Nature (1996), supra; S. Korolev et al., Cell, (1997), supra]. Mutation of a conserved arginine in this motif in UvrD increases the ATP Km by 37-fold [M. C. Hall et al., J. Biol. Chem., 272, pp. 18614-18620 (1997)].

In HCV helicase either another protein segment which is not in the current structure substitutes for motif IV or the adenosine ring binds elsewhere. Residues from the putative motif IV in HCV helicase include Ser-370 and Lys-371, which contact the DNA via a water-mediated hydrogen bond and a backbone interaction, respectively. Therefore sequences corresponding to motif IV in superfamily I and superfamily II helicases occupy different regions and appear to have different functions. We suggest that a new motif, designated IVa, be used to describe residues corresponding to the putative HCV helicase motif IV. In *E. coli* UvrD, motif IVa may correspond to the sequence RSNAQSRVL (residues 355-363).

Proposed domain closure and translocation

Conserved, basic residues from motif VI are positioned across the interdomain cleft from the expected location of the ATP γ phosphate in HCV helicase. A very similar situation is observed in the structures of the adenylate kinases, where basic residues lie across a cleft from the ATP binding site. Binding of ATP (or analogs) to these kinases leads to a conformational change in the enzyme, resulting in the burial of previously solvent-exposed phosphates [T. Bilderback et al., Biochemistry, 35, pp. 6100-6106 (1996)]. Mutation of these conserved basic residues in adenylate kinase results in an open structure with poor catalytic activity [G. E. Schulz, Faraday Discuss., 93, pp. 85-93 (1992)].

We propose that an analogous closure occurs between domains 1 and 2 of HCV helicase upon ATP binding. This closure could be driven by interaction of basic residues in motif VI with the ATP phosphates. Sequence and structural conservation of these basic residues in motif VI among superfamily I and II helicases suggests that domain closure upon ATP binding is a general feature of these enzymes.

Gln-460 and His-293, from motifs VI and II respectively, lie on opposite sides of the interdomain

cleft and possibly serve as gatekeepers, altering the equilibrium between the open and closed forms based on the binding of polynucleotide. Potential interaction of residues in these positions was predicted by the observation that helicases with the DExH motif II sequence usually contain a glutamine in motif VI, whereas those with a DEAD sequence contain a histidine [A. Gorbalenya et al., Curr. Opin. Struct. Biol. (1993), supra].

There is structural evidence that the linkage of the second domain in HCV helicase to the rest of the protein is flexible. In the HCV helicase structure reported by N. Yao et al., Nat. Struct. Biol. (1997), supra, the differences between the two molecules in the asymmetric unit can be attributed to a rotation of domain 2 by a few degrees. The relatively minor movement of domain 2 observed in their structures probably reflects changes in the local environment in the crystals. We propose a much more substantial conformational change would occur when the enzyme binds ATP or suitable analog. Our crystallographic results indicate that there are significant movements of this domain in different crystal forms. A conformational change could explain the observed two-stage kinetics of ATP binding to Rep where

rapid initial binding is followed by a much slower step, leading to tighter binding [K. J. Moore et al., Biochemistry, 33, pp. 14550-14564 (1994)]. Evidence for conformational changes have been observed for Rep and helicase II based on alterations in protease sensitivity upon nucleotide binding [K. Chao et al., J. Biol. Chem., 265, pp. 1067-1076 (1990)]. Binding of ATP to PcrA helicase has also been proposed to lead to a conformational change of the enzyme [H. S. Subramanya et al., Nature (1996), supra].

Large conformational changes in a DNA metabolizing enzyme are not unique, as they have been seen in the structures of mRNA capping enzyme in the presence of GTP [K. Hakansson et al., Cell, 89, pp. 545-553 (1997)]. In these structures the guanosine nucleotide is bound to the N-terminal domain with the phosphates located near the interface with the C-terminal domain. In the "open" conformation these domains are separated by a 10-13 Å cleft. Several residues which are highly conserved among mRNA capping enzymes are located in the C-terminal domain, including Arg-295 and Arg-298.

In the "closed" conformation, these residues are relocated by approximately 10 Å and are bound to the GTP β and γ phosphates. Closures of large interdomain

clefts have also been proposed in the structurally homologous ATP-dependent DNA ligases, of which one structure has been solved in the open conformation [H. S. Subramanya et al., Cell, 85, pp. 607-615 (1996)].

The second domain of HCV helicase also interacts with the single-stranded polynucleotide. One could envision that movement of this domain results in concomitant movement of the nucleic acid substrate relative to the protein. Interactions between residues in domain 2 such as Val-432 and Thr-448 and the bases at the 5' end of the single stranded nucleic acid binding site would lead to translocation of the polynucleotide in the 5' to 3' direction as domain 2 closes.

Trp-501 in domain 3 stacks with a base near the 3' end of the single stranded oligonucleotide and disrupts stacking with neighboring bases. Closure of the interdomain cleft would force several bases to slip past Trp-501. Hydrolysis of ATP would then result in opening of the cleft and release of ADP. The orientation of Trp-501 favors movement of the polynucleotide in only the 5' to 3' direction such that opening of the cleft results in net movement of domain 2 in a 3' to 5' direction. By this mechanism the translocation reaction of the helicase resembles a ratchet. A general ratchet-like mechanism

has been proposed for the RecB helicase based on conformational changes observed by protease mapping [R. J. Phillips et al., Mol. Gen. Genet., 254, pp. 319-329 (1997)].

Such a model suggests that a single ATP hydrolysis event can result in protein translocation of several bases along a polynucleotide. Studies with the UvrD DNA helicase have demonstrated that the enzyme is capable of translocating more than one base per reaction cycle [J. A. Ali et al., Science, 275, pp. 377-380 (1997)], although the number of ATP hydrolysis events per observed reaction cycle was unknown in this experiment. Our model is consistent with predictions that helicases need not actively unwind the double-stranded substrate, but can function by capturing the single-stranded regions which arise due to thermal fluctuations at the fork [Y. Z. Chen et al., J. Biomol. Struct. Dyn., 10, pp. 415-427 (1992)]. The translocation process proposed here would thus be considered an active process while the melting of double stranded structure at the fork would be passive.

The mechanism which we propose is substantially different from one described for the Rep helicase by Wong and Lohman [I. Wong et al., Science, 256, pp. 350-355 (1992)] and recently advanced in a paper describing the

3.0 and 3.2 Å structures of Rep bound to single-stranded DNA [S. Korolev et al., Cell (1997), supra]. As we previously noted there is overall structural similarity between domains 1 and 2 of HCV helicase and domains 1A and 2A of Rep. Important to our proposed mechanism, these two domains contain all the motifs conserved among DNA/RNA helicase sequences listed in Figure 9A. In HCV helicase, there is no structural equivalent of Rep domain 2B which has been proposed to have a critical role in the active rolling mechanism [S. Korolev et al., Cell (1997), supra].

EXAMPLE 5

Assays

A. Helicase assay

The standard 3'-tailed double-stranded RNA/DNA hybrid was prepared as described as follows. The long 98-nucleotide ("nt") RNA template was transcribed from a BsrBI-digested plasmid pSP65 (Promega, Madison, WI) in the presence of [α-^{32}P-GTP] (New England Nuclear, Boston, MA). The short 34-nt DNA release strand corresponds to a SP6 RNA transcript from a BamHI-digested pSP64 (Promega).

Standard helicase reactions (20 µl) were carried out as follows. HCV NS3 helicase (0.3 or 1 nM)

was added to a mixture of 25 mM morpholinepropanesulfonic acid (MOPS)-NaOH (pH 6.5), 1 mM ATP, 0.5 mM $MnCl_2$, 2 mM dithiothreitol (DTT), 0.1 mg of bovine serum albumin (BSA) per ml, 4 units of RNasin (Promega), and 5 nM of 3'-tailed double-stranded RNA/DNA hybrid substrate. Mixtures were incubated for 20 min at 37°C and stopped by the addition of 5 liters of 5X loading buffer [100 mM Tris-Cl (pH7.5), 20 mM EDTA, 50 % glycerol, 0.5 % SDS, 0.1 % NP-40, 0.1 % bromophenol blue, and 0.1 % xylene cyanole). The reactions were then electrophoresed on 10% PAGE with 0.5x TBE and 0.1 % SDS. Gels were dried and exposed using Fuji 1500 phosphorimager (Fuji, Stamford, CT). Helicase activity was determined by radioactivity of the double-stranded substrate and single-stranded template.

First, we characterized unwinding activity of the purified wild type NS3 helicase domain protein with regarding to the following parameters: protein concentration, incubation time course, incubation temperature, ATP concentration, pH, monovalent cation (Na^+), and divalent cation (Mn^{2+} and Mg^{2+}) (Fig. 11).

The helicase unwinding activity increased as the protein concentration or incubation time increased (Fig. 11A). At 0.1 nM of the NS3 helicase, the reaction

was almost linear with regard to the incubation time up to 30 min (Fig. 11A). Several NS3 helicase mutants purified by the same chromatograph method did not show any unwinding activity (see Table 1 and Example 6, below), indicating that the unwinding activity shown here is due to the purified HCV NS3 helicase, not containment proteins from *E. coli*.

Higher incubation temperature also led to more rapid unwinding of substrate (Fig. 11B), presumably due to lower energy required for break-down of hydrogen bonds between two strands at higher temperature. The unwinding activity of this NS3 helicase domain was optimal at pH 6.5, with a very narrow pH window of being active (Fig. 11C).

In addition, the unwinding reaction was very sensitive to the monovalent cation, such as Na^+ (Fig. 11D). Addition of 25 mM NaCl decreased the unwinding activity to about 15% of that in the absence of extra NaCl.

This helicase activity was absolutely dependent on the presence of ATP (Fig. 11E) or any other type of nucleotide triphosphate (NTP) (data not shown). The unwinding activity increased almost linearly as the concentration of ATP increased up to 1 mM (Fig. 11E).

However, at 5 mM of ATP, the unwinding activity is lower than that at 1 mM of ATP, probably due to inhibition of extra Na^+ brought in with the ATP.

The helicase activity also absolutely require the presence of divalent cations, such as Mn^{2+} or Mg^{2+} (Fig. 11F). However, if the concentration of divalent cation was higher than that of ATP, inhibition of the helicase activity was observed. At equal concentration of ATP and divalent cation (1 mM or 5 mM), Mn^{2+} showed higher unwinding activity than Mg^{2+} (Fig. 11F).

B. Single Stranded RNA binding assay

The binding of single stranded RNA ("ssRNA") to the HCV NS3 helicase was measured by a nitrocellulose filter binding assay. A 34-nt RNA transcript was generated from BamHI-digested pSP64 plasmid using SP6 RNA polymerase in the presence of [α-^{32}P-GTP]. Standard ssRNA binding reactions (40 µl) were carried out as follows.

HCV NS3 helicase domain protein (6.25 nM) was added to a mixture of 25 mM morpholinepropanesulfonic acid (MOPS)-NaOH (pH 7.0), 2 mM dithiothreitol (DTT), 0.1 mg of bovine serum albumin (BSA) per ml, 4 units of RNasin (Promega), and 5 nM of [^{32}P]-ssRNA substrate.

Mixtures were incubated for 15 min at 30°C and filtered through a pre-wet nitrocellulose membrane. The filter were washed twice with washing buffer [50 mM MOPS-NaOH (pH 7.0) and 1 mM EDTA], dried and quantified in scintillation counter.

Next, we determine several parameters in the ssRNA binding to the purified NS3 helicase using a filter binding assay (Fig. 12). The association of ^{32}P-labeled ssRNA to the NS3 helicase was very quick, usually close to completion within a couple minutes of incubation (data not shown). As shown in Fig. 12A, binding of ssRNA to the NS3 helicase is protein concentration-dependent. Under 8 nM of the NS3 helicase, the amount of ssRNA bound is a linear function of protein concentration (Fig. 12A, insert), and there is 0.445 molecule of ssRNA bound for every molecule of the NS3 helicase being present in the reaction. The maximal amount of ssRNA binding achieved in this reaction is about 94%. The K_d of the ssRNA-NS3 helicase complex is calculated to be 5.18 nM, at which the 50% of maximal binding of ssRNA to the NS3 helicase domain was observed.

We also measured the off rate constant of pre-formed ssRNA-NS3 helicase complex (Fig. 12B). In this case, ^{32}P-labeled ssRNA was incubated with the NS3

helicase protein was incubated together for 15 minutes to allow the formation of ^{32}P-ssRNA-NS3 helicase complex. Then 50-fold excess of ^{3}H-labeled ssRNA with the same sequence was added to the reaction so that any ^{32}P-labeled ssRNA dissociated from the complex with the NS3 helicase would have very little chance to re-associate with the NS3 protein again. The dissociation rate was determined to be 1.52×10^{-2} min-1.

We also examined effect of pH, monovalent (Na^+) and divalent (Mn^{2+}) cations on the ssRNA binding to the NS3 helicase. In contrast to the unwinding activity, ssRNA binding of the NS3 helicase was less sensitive to the pH change (Fig. 12C). The optimal binding was observed at pH 7.0, although ssRNA binding did not change significantly between pH 6.5 to 8.0. NaCl (Fig. 12D) and $MgCl_2$ (Fig. 12E) has an inhibitory effect on the ssRNA binding, although this inhibition curve as a function of salt concentration is not as sharp as that on unwinding activity.

C. <u>ATPase assay</u>

ATPase was measured by hydrolysis of ATP to ADP using a thin layer chromatography method [J.K. Tamura et. al., <u>Virology</u>, 193, pp.1-10 (1993)]. Standard ssRNA

binding reactions (10 µl) were carried out as follows. HCV NS3 helicase domain protein (2 nM) was added to a mixture of 50 mM morpholinepropanesulfonic acid (MOPS)-NaOH (pH 7.0), 0.1 mM ATP, 2.5 µCi of [α-^{32}P-ATP] (NEN), 0.5 mM $MgCl_2$, 1 mM dithiothreitol (DTT), 0.1 mg of bovine serum albumin (BSA) per ml, and in the presence or absence of 5 µM poly U (Uridine concentration) (Pharmacia). Mixtures were incubated for 30 min at 37°C and terminated by addition of EDTA to a final concentration of 20 mM. 0.5 µl of the reaction was spotted on a polyethyleneimine-cellulose plate, ATP and ADP were separated in 375 mM potassium phosphate (pH 3.5) and quantified by Fuji phosphorimager.

ATPase activity of the purified NS3 helicase was examined using this method. As shown in Fig. 13, this NS3 helicase domain has a basal ATPase activity in the absence of any polynucleotide, and the ATPase activity was stimulated up to 11-fold in the presence of poly(U). The order of ATPase stimulation by polynucleotides is poly(U) > poly(C) > poly(A) > poly(G) (data not shown).

EXAMPLE 6

Structure-Based Mutagenesis Study of RNA-Binding Residues of the NS3 Helicase

Mutagenesis experiments were performed to examine the roles of several residues predicted to be important in the NS3 helicase:oligonucleotide interaction based upon the crystal structure of that complex.

Ser231, Thr269, Ser370 and Thr411 formed direct water-mediated hydrogen bonds with the phosphate groups of the bound oligonucleotide. We replaced each one of these amino acids individually with alanine (see Example 1) and observed the effect of that mutation on various helicase activities. Alanine substitution at Ser231 or Ser370 had no observable effect on basal or polyU-stimulated ATPase activity, unwinding activity or ssRNA binding activity as compared to wild type helicase (see Table 1, below). Thus, it was concluded that those amino acids were not essential to define the oligonucleotide binding pocket in NS3 helicase.

In contrast, alanine substitution at Thr269 or Thr411 decreased the ssRNA binding to 20% of wild type level and completely abolished both polyU-stimulated ATPase activity and unwinding activity. Interestingly, basal ATPase activity was unaffected by either of these mutations.

The crystal structure also suggested that the side chain of Trp501 interacts with the bound

oligonucleotide. Substitution of this Trp with either Ala or Leu resulted in decreased ssRNA binding and abolished polyU-stimulated ATPase activity and unwinding activity, although basal ATPase activity was unaffected. In contrast a Trp501-to-Phe mutation did not affect basal ATPase, unwinding and ssRNA binding activities. This mutant was, however, less sensitive to polyU-stimulation of ATPase activity as compared to the wild type helicase. Surprisingly, the ATPase activity of this mutant when stimulated by other polynucleotides, such as polyC, was similar to that of the wild type.

Table 1. Mutational Study of Amino Acids in the RNA Binding Site of HCV NS3 Helicase

Amino Acid Mutation	*Basal ATPase Activity (% of basal WT level)*	*Poly-U Stimulated ATPase Activity (% of basal WT level)*	*ssRNA Binding Activity (% of WT level)*	*ds RNA/DNA Unwinding Activity (% of WT level)*
None (WT)	**100**	**823**	**100**	**100**
S231->A	**260**	**709**	**121**	**99.8**
T269->A	**60**	**47**	**21**	**1**
S370->A	**104**	**694**	**124**	**109**
T411->A	**274**	**205**	**24**	**0.25**
W501->F	**99**	**197**	**100**	**112**
W501->L	**114**	**47**	**21**	**0.07**
W501->A	**101**	**49**	**40**	**0.36**

Based upon these studies, it is apparent that Thr269, Thr411 and Trp501 are key residues for oligonucleotide binding. As indicated above, Thr269 and Trp501 make direct contacts with dU8. The minimal helicase amino acids which define the pocket in which dU8

lies are Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501 and Tyr502. Thus, any compound which fits into a pocket comprising the structural coordinates ± a root mean square of 1.5 Å or less from the backbone atoms of these amino acids is a potential inhibitor of the NS3 helicase.

Additional amino acids that are located within 4 Å to 8 Å from the dU8 pocket are Pro230, Val256, Thr298, Ala497, Lys551, Gln552, Gly554, Glu555, Asn556 and Pro558. Thus, the combination of these amino acids with those above further define the dU8 pocket.

Based upon the crystal structure and these mutagenesis experiments, it is clear that Thr411 makes direct contact with dU4 and is a key residue in the U4 binding pocket. Other amino acids that are close enough to that U4 pocket to define its shape are His369, Ser370, Lys371, Tyr392, Arg393, Asp412, Ala413, Cys431, Val432, Gln434, Ile446, Thr448, Arg461, Glu493, Glu555, Asn556 and Phe557.

EXAMPLE 7

Structure-Based Mutagenesis Study of ATP-Binding Residues of the NS3 Helicase

Mutagenesis experiments were performed to examine the roles of several residues predicted to be

important in the NS3 helicase:ATP interaction based upon the crystal structure of that complex.

The mutations were achieved by the methods described in Example 1.

Table 2. Mutational Study of Amino Acids in the ATP Binding Site of HCV NS3 Helicase

Mutation	Basal ATPase (% of basal wt level)	Poly U-stimulated ATPase (% of basal wt level)	ssRNA binding (% of wt level)	dsRNA /DNA unwinding (% of wt level)
wild-type	100	581	100	100
Q460->A	23	32	97	3
R461->A	140	193	57	2
R462->A	247	337	99	81
R464->A	33	21	105	<0.01
R467->A	7	14	116	<0.05

In our model, R464 and R467 were predicted to bind to the γ- and α- phosphate groups of NTP, respectively. This is in contrast to what has previously been reported in the art, wherein these residues were predicted to be involved in RNA binding [T. Yao et al., Nat. Struct. Biol., 4, pp. 463-467 (1997); C. Hyun-Soo et al., J. Biol. Chem., 273, pp. 15045-15052 (1998)].

Two individual mutations, R464->A and R467->A, showed very low basal and polyU-stimulated ATPase activities. Although they had normal RNA binding ability, which suggested that the mutated protein has a proper fold, helicase unwinding activity was almost non-existent in these two mutant proteins, presumably due to the loss of NTPase activity. These results indicated

that these two Arg residues are critical for NTPase activity.

The Q460->A mutation had a similar effect as two above-mentioned Arg-to-Ala mutations. This Gln was predicted to interact with and maintain the proper conformation of the imidazole ring of His-293 of the DECH motif.

The R461->A mutation led to lower RNA binding and less polyU stimulation of ATPase activity, which resulted in a very low helicase unwinding activity.

The R462->A mutation had no major effect on any of these four activities as predicted.

While we have hereinbefore presented a number of embodiments of this invention, it is apparent that my basic construction can be altered to provide other embodiments which utilize the methods of this invention. Therefore, it will be appreciated that the scope of this invention is to be defined by the claims appended hereto rather than the specific embodiments which have been presented hereinbefore by way of example.

CLAIMS

We claim:

1. A crystallizable composition comprising an HCV NS3 helicase protein and an oligonucleotide.

2. The composition according to claim 1, wherein said HCV NS3 helicase comprises amino acids 167-631 of SEQ ID NO:1 and wherein said oligonucleotide is a single stranded polynucleotide of between 6 and 12 nucleotides in length.

3. A crystallized complex comprising an HCV NS3 helicase protein and an oligonucleotide.

4. The crystallized complex according to claim 3, wherein said oligonucleotide is a single stranded polynucleotide of between 6 and 12 nucleotides in length.

5. A method of producing a crystallized complex comprising an HCV NS3 helicase and an oligonucleotide comprising the steps of:

a. obtaining a crystallizable composition comprising an NS3 helicase protein and an oligonucleotide in a molar ratio of between 1:5 and 5:1; and

b. subjecting said composition to conditions which promote crystallization.

6. The method according to claim 5, wherein said HCV NS3 helicase comprises amino acids 167-631 of SEQ ID NO:1 and wherein said oligonucleotide is a single stranded polynucleotide of between 6 and 12 nucleotides in length.

7. A computer for producing a three-dimensional representation of:

a. a molecule or molecular complex, wherein said molecule or molecular complex comprises a binding pocket defined by structure coordinates of NS3 amino acids Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501 and Tyr502 according to Figure 1; or

b. a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from

the backbone atoms of said amino acids of not more than 1.5Å, wherein said computer comprises:

(i) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said data comprises the structure coordinates of NS3 amino acids Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501 and Tyr502 according to Figure 1;

(ii) a working memory for storing instructions for processing said machine-readable data;

(iii) a central-processing unit coupled to said working memory and to said machine-readable data storage medium for processing said machine readable data into said three-dimensional representation; and

(iv) a display coupled to said central-processing unit for displaying said three-dimensional representation.

8. The computer according to claim 7, wherein said computer produces a three-dimensional representation of:

a) a molecule or molecular complex comprising a binding pocket defined by the structure coordinates of NS3 helicase amino acids Val232, Thr254,

Gly255, Thr269, Gly271, Lys272, Ala275, Trp501, Tyr502, Pro230, Val256, Thr298, Ala497, Lys551, Gln552, Gly554, Glu555, Asn556 and Pro558, according to Figure 1; or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å; and

wherein said machine readable data comprises the structure coordinates of NS3 amino acids Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501, Tyr502, Pro230, Val256, Thr298, Ala497, Lys551, Gln552, Gly554, Glu555, Asn556 and Pro558, according to Figure 1.

9. A computer for producing a three-dimensional representation of:

a) a molecule or molecular complex comprising a binding pocket defined by the structure coordinates of NS3 helicase amino acids His369, Ser370, Lys371, Tyr392, Arg393, Thr411, Asp412, Ala413, Cys431, Val432, Gln434, Ile446, Thr448, Arg461, Glu493, Glu555, Asn556 and Phe557, according to Figure 1; or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a

binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, wherein said computer comprises:

(i) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said data comprises the structure coordinates of NS3 amino acids His369, Ser370, Lys371, Tyr392, Arg393, Thr411, Asp412, Ala413, Cys431, Val432, Gln434, Ile446, Thr448, Arg461, Glu493, Glu555, Asn556 and Phe557, according to Figure 1;

(ii) a working memory for storing instructions for processing said machine-readable data;

(iii) a central-processing unit coupled to said working memory and to said machine-readable data storage medium for processing said machine readable data into said three-dimensional representation; and

(iv) a display coupled to said central-processing unit for displaying said three-dimensional representation.

10. A computer for producing a three-dimensional representation of:

a) a molecule or molecular complex comprising a binding pocket defined by the structure

coordinates of NS3 helicase amino acids Pro205, Thr206, Gly207, Ser208, Gly209, Lys210, Ser211, Thr212, Lys213, Asn229, Ala234, Gly237, Phe238, Tyr241, Asp290, Glu291, His293, Thr322, Ala323, Thr324, Gln460, Gly463, Arg464 and Arg467, according to Figure 1; or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Â, wherein said computer comprises:

(i) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said data comprises the structure coordinates of NS3 amino acids Pro205, Thr206, Gly207, Ser208, Gly209, Lys210, Ser211, Thr212, Lys213, Asn229, Ala234, Gly237, Phe238, Tyr241, Asp290, Glu291, His293, Thr322, Ala323, Thr324, Gln460, Gly463, Arg464 and Arg467, according to Figure 1;

(ii) a working memory for storing instructions for processing said machine-readable data;

(iii) a central-processing unit coupled to said working memory and to said machine-readable data storage medium for processing said machine readable data into said three-dimensional representation; and

(iv) a display coupled to said central-processing unit for displaying said three-dimensional representation.

11. The computer according to any one of claims 7 to 10, wherein said computer produces a three-dimensional representation of:

a. a molecule or molecular complex defined by structure coordinates of all of the NS3 amino acids set forth in Figure 1, or

b. a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å; and

wherein said machine readable data contains the coordinates of all of the NS3 helicase amino acids set forth in Figure 1.

12. A computer for determining at least a portion of the structure coordinates corresponding to X-ray diffraction data obtained from a molecule or molecular complex, wherein said computer comprises:

(a) a machine-readable data storage

medium comprising a data storage material encoded with machine-readable data, wherein said data comprises at least a portion of the structural coordinates of NS3 helicase according to Figure 1;

(b) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said data comprises X-ray diffraction data obtained from said molecule or molecular complex;

(c) a working memory for storing instructions for processing said machine-readable data of (a) and (b);

(d) a central-processing unit coupled to said working memory and to said machine-readable data storage medium of (a) and (b) for performing a Fourier transform of the machine readable data of (a) and for processing said machine readable data of (b) into structure coordinates; and

(e) a display coupled to said central-processing unit for displaying said structure coordinates of said molecule or molecular complex.

13. The computer according to claim 12, wherein said molecule or molecular complex comprises a

polypeptide having helicase activity.

14. A method for evaluating the potential of a chemical entity to associate with:

a) a molecule or molecular complex comprising a binding pocket defined by structure coordinates of NS3 helicase amino acids Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501 and Tyr502 according to Figure 1, or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Δ comprising the steps of:

i) employing computational means to perform a fitting operation between the chemical entity and a binding pocket of the molecule or molecular complex; and

ii) analyzing the results of said fitting operation to quantify the association between the chemical entity and the binding pocket.

15. The method according to claim 14, wherein said method evaluates the potential of a chemical entity to associate with:

a) a molecule or molecular complex comprising a binding pocket defined by structure coordinates of NS3 helicase amino acids Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501, Tyr502, Pro230, Val256, Thr298, Ala497, Lys551, Gln552, Gly554, Glu555, Asn556 and Pro558 according to Figure 1, or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Δ.

16. A method for evaluating the potential of a chemical entity to associate with:

a) a molecule or molecular complex comprising a binding pocket defined by structure coordinates of NS3 helicase amino acids His369, Ser370, Lys371, Tyr392, Arg393, Thr411, Asp412, Ala413, Cys431, Val432, Gln434, Ile446, Thr448, Arg461, Glu493, Glu555, Asn556 and Phe557 according to Figure 1, or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than

1.5 Å comprising the steps of:

i) employing computational means to perform a fitting operation between the chemical entity and a binding pocket of the molecule or molecular complex; and

ii) analyzing the results of said fitting operation to quantify the association between the chemical entity and the binding pocket.

17. A method for evaluating the potential of a chemical entity to associate with:

a) a molecule or molecular complex comprising a binding pocket defined by structure coordinates of NS3 helicase amino acids Pro205, Thr206, Gly207, Ser208, Gly209, Lys210, Ser211, Thr212, Lys213, Asn229, Ala234, Gly237, Phe238, Tyr241, Asp290, Glu291, His293, Thr322, Ala323, Thr324, Gln460, Gly463, Arg464 and Arg467 according to Figure 1, or

b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å comprising the steps of:

i) employing computational means to perform a fitting operation between the chemical entity and a

binding pocket of the molecule or molecular complex; and

ii) analyzing the results of said fitting operation to quantify the association between the chemical entity and the binding pocket.

18. The method according to any one of claims 14 to 17, wherein said method evaluates the potential of a chemical entity to associate with a molecule or molecular complex:

a. defined by structure coordinates of all of the NS3 helicase amino acids, as set forth in Figure 1, or

b. a homologue of said molecule or molecular complex having a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Δ.

19. A method for identifying a potential agonist or antagonist of a molecule comprising a NS3 helicase U8-like binding pocket comprising the steps of:

a. using the atomic coordinates of Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501 and Tyr502 according to Figure 1 ± a root mean square deviation from the backbone atoms of said amino

acids of not more than 1.5Å, to generate a three-dimensional structure of molecule comprising a NS3 helicase U8-like binding pocket;

b. employing said three-dimensional structure to design or select said potential agonist or antagonist;

c. synthesizing said agonist or antagonist; and

d. contacting said agonist or antagonist with said molecule to determine the ability of said potential agonist or antagonist to interact with said molecule.

20. The method according to claim 19, wherein the atomic coordinates used in step a. comprise Val232, Thr254, Gly255, Thr269, Gly271, Lys272, Ala275, Trp501, Tyr502, Pro230, Val256, Thr298, Ala497, Lys551, Gln552, Gly554, Glu555, Asn556 and Pro558 according to Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

21. A method for identifying a potential agonist or antagonist of a molecule comprising a NS3 helicase U4-like binding pocket comprising the steps of:

a. using the atomic coordinates of His369, Ser370, Lys371, Tyr392, Arg393, Thr411, Asp412, Ala413, Cys431, Val432, Gln434, Ile446, Thr448, Arg461, Glu493, Glu555, Asn556 and Phe557 according to Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, to generate a three-dimensional structure of molecule comprising a NS3 helicase U8-like binding pocket;

b. employing said three-dimensional structure to design or select said potential agonist or antagonist;

c. synthesizing said agonist or antagonist; and

d. contacting said agonist or antagonist with said molecule to determine the ability of said potential agonist or antagonist to interact with said molecule.

22. A method for identifying a potential agonist or antagonist of a molecule comprising a NS3 helicase ATP-like binding pocket comprising the steps of:

a. using the atomic coordinates of Pro205, Thr206, Gly207, Ser208, Gly209, Lys210, Ser211, Thr212, Lys213, Asn229, Ala234, Gly237, Phe238, Tyr241,

Asp290, Glu291, His293, Thr322, Ala323, Thr324, Gln460, Gly463, Arg464 and Arg467 according to Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Δ, to generate a three-dimensional structure of molecule comprising a NS3 helicase U8-like binding pocket;

b. employing said three-dimensional structure to design or select said potential agonist or antagonist;

c. synthesizing said agonist or antagonist; and

d. contacting said agonist or antagonist with said molecule to determine the ability of said potential agonist or antagonist to interact with said molecule.

23. The method according to any one of claims 19 to 22, wherein in step a., the atomic coordinates of all the amino acids of NS3 helicase according to Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å are used.

24. A method of obtaining structural information about a molecule or molecular complex whose structure is unknown comprising the steps of:

a) crystallizing said molecule or molecular complex of unknown structure;

b) generating X-ray diffraction data from said crystallized molecule or molecular complex; and

c) applying at least a portion of the structure coordinates set forth in Figure 1 to the X-ray diffraction data to generate a three-dimensional electron density map of the molecule or molecular complex whose structure is unknown.

HCV NS3 HELICASE COORDINATES

		Atom Type	Resid	#	X	Y	Z	OCC	B
ATOM	1	N	PRO	190	-0.567	24.363	16.753	1.00	49.28
ATOM	2	CD	PRO	190	-0.755	25.375	17.807	1.00	48.44
ATOM	3	CA	PRO	190	-0.399	23.026	17.339	1.00	49.21
ATOM	4	CB	PRO	190	-0.793	23.252	18.793	1.00	48.67
ATOM	5	CG	PRO	190	-0.283	24.643	19.036	1.00	48.14
ATOM	6	C	PRO	190	-1.288	21.990	16.644	1.00	49.61
ATOM	7	O	PRO	190	-2.520	22.007	16.772	1.00	49.44
ATOM	8	N	PRO	191	-0.669	21.098	15.857	1.00	49.77
ATOM	9	CD	PRO	191	0.761	21.088	15.505	1.00	50.59
ATOM	10	CA	PRO	191	-1.389	20.053	15.125	1.00	49.68
ATOM	11	CB	PRO	191	-0.296	19.432	14.245	1.00	49.43
ATOM	12	CG	PRO	191	0.723	20.544	14.109	1.00	50.11
ATOM	13	C	PRO	191	-2.024	19.007	16.033	1.00	49.16
ATOM	14	O	PRO	191	-1.368	18.447	16.911	1.00	49.03
ATOM	15	N	ALA	192	-3.309	18.751	15.823	1.00	48.24
ATOM	16	CA	ALA	192	-4.000	17.745	16.616	1.00	47.12
ATOM	17	CB	ALA	192	-5.477	17.713	16.265	1.00	47.93
ATOM	18	C	ALA	192	-3.356	16.408	16.283	1.00	45.46
ATOM	19	O	ALA	192	-2.803	16.234	15.193	1.00	44.90
ATOM	20	N	VAL	193	-3.398	15.481	17.230	1.00	43.63
ATOM	21	CA	VAL	193	-2.823	14.164	17.009	1.00	42.13
ATOM	22	CB	VAL	193	-2.825	13.322	18.299	1.00	40.58
ATOM	23	CG1	VAL	193	-2.060	12.023	18.080	1.00	39.57
ATOM	24	CG2	VAL	193	-2.217	14.124	19.442	1.00	38.30
ATOM	25	C	VAL	193	-3.641	13.482	15.909	1.00	42.80
ATOM	26	O	VAL	193	-4.810	13.132	16.109	1.00	42.17
ATOM	27	N	PRO	194	-3.033	13.309	14.724	1.00	42.99
ATOM	28	CD	PRO	194	-1.601	13.536	14.488	1.00	43.90
ATOM	29	CA	PRO	194	-3.638	12.690	13.546	1.00	43.17
ATOM	30	CB	PRO	194	-2.493	12.691	12.536	1.00	43.02
ATOM	31	CG	PRO	194	-1.571	13.753	13.016	1.00	43.69
ATOM	32	C	PRO	194	-4.068	11.265	13.819	1.00	43.70
ATOM	33	O	PRO	194	-3.519	10.595	14.691	1.00	44.16
ATOM	34	N	ALA	195	-5.031	10.794	13.038	1.00	43.76
ATOM	35	CA	ALA	195	-5.522	9.433	13.176	1.00	43.44
ATOM	36	CB	ALA	195	-6.782	9.247	12.327	1.00	44.50
ATOM	37	C	ALA	195	-4.422	8.466	12.732	1.00	42.59
ATOM	38	O	ALA	195	-4.320	7.345	13.235	1.00	43.20
ATOM	39	N	SER	196	-3.607	8.914	11.783	1.00	41.07
ATOM	40	CA	SER	196	-2.507	8.117	11.255	1.00	40.13
ATOM	41	CB	SER	196	-2.859	7.604	9.851	1.00	41.51
ATOM	42	CG	SER	195	-3.572	8.583	9.106	1.00	43.93
ATOM	43	C	SER	196	-1.225	8.957	11.233	1.00	37.38
ATOM	44	O	SER	196	-1.274	10.181	11.393	1.00	36.47
ATOM	45	N	PHE	197	-0.082	8.303	11.037	1.00	35.00
ATOM	46	CA	PHE	197	1.193	9.017	11.014	1.00	31.57
ATOM	47	CB	PHE	197	2.373	8.079	10.744	1.00	28.81
ATOM	48	CG	PHE	197	3.697	8.794	10.693	1.00	25.09
ATOM	49	CD1	PHE	197	4.343	9.162	11.863	1.00	23.41
ATOM	50	CD2	PHE	197	4.254	9.167	9.482	1.00	23.23
ATOM	51	CE1	PHE	197	5.505	9.887	11.824	1.00	21.81
ATOM	52	CE2	PHE	197	5.420	9.894	9.437	1.00	21.64
ATOM	53	CZ	PHE	197	6.045	10.256	10.606	1.00	22.04

ATOM	54	C	PHE	197	1.262	10.163	10.020	1.00	30.70
ATOM	55	O	PHE	197	1.089	9.965	8.816	1.00	31.02
ATOM	56	N	GLN	198	1.582	11.345	10.536	1.00	30.64
ATOM	57	CA	GLN	198	1.731	12.550	9.732	1.00	30.20
ATOM	58	CB	GLN	198	0.478	13.438	9.818	1.00	33.70
ATOM	59	CG	GLN	198	-0.893	12.720	9.747	1.00	38.79
ATOM	60	CD	GLN	198	-1.331	12.268	8.350	1.00	41.73
ATOM	61	OE1	GLN	198	-2.254	11.462	8.218	1.00	44.20
ATOM	62	NE2	GLN	198	-0.696	12.802	7.310	1.00	44.35
ATOM	63	C	GLN	198	2.921	13.340	10.279	1.00	28.49
ATOM	64	O	GLN	198	3.341	13.148	11.423	1.00	27.20
ATOM	65	N	VAL	199	3.485	14.191	9.431	1.00	28.09
ATOM	66	CA	VAL	199	4.595	15.074	9.786	1.00	27.30
ATOM	67	CB	VAL	199	5.798	14.949	8.803	1.00	27.93
ATOM	68	CG1	VAL	199	6.783	16.106	9.018	1.00	26.84
ATOM	69	CG2	VAL	199	6.510	13.607	8.984	1.00	27.42
ATOM	70	C	VAL	199	3.989	16.464	9.624	1.00	26.70
ATOM	71	O	VAL	199	3.425	16.784	8.579	1.00	26.24
ATOM	72	N	ALA	200	4.115	17.298	10.640	1.00	26.58
ATOM	73	CA	ALA	200	3.538	18.624	10.574	1.00	25.57
ATOM	74	CB	ALA	200	2.364	18.725	11.544	1.00	24.63
ATOM	75	C	ALA	200	4.567	19.677	10.906	1.00	25.17
ATOM	76	O	ALA	200	5.569	19.400	11.558	1.00	24.12
ATOM	77	N	HIS	201	4.306	20.891	10.442	1.00	25.38
ATOM	78	CA	HIS	201	5.178	22.022	10.698	1.00	25.85
ATOM	79	CB	HIS	201	5.417	22.812	9.413	1.00	24.66
ATOM	80	CG	HIS	201	6.130	22.041	8.353	1.00	24.83
ATOM	81	CD2	HIS	201	5.683	21.125	7.461	1.00	26.76
ATOM	82	ND1	HIS	201	7.480	22.171	8.124	1.00	24.29
ATOM	83	CE1	HIS	201	7.838	21.367	7.139	1.00	27.15
ATOM	84	NE2	HIS	201	6.767	20.722	6.719	1.00	28.31
ATOM	85	C	HIS	201	4.469	22.927	11.689	1.00	26.56
ATOM	86	O	HIS	201	3.264	23.163	11.556	1.00	27.65
ATOM	87	N	LEU	202	5.191	23.399	12.698	1.00	26.07
ATOM	88	CA	LEU	202	4.601	24.317	13.659	1.00	25.58
ATOM	89	CB	LEU	202	4.621	23.756	15.085	1.00	25.67
ATOM	90	CG	LEU	202	4.182	24.740	16.183	1.00	25.11
ATOM	91	CD1	LEU	202	2.710	25.088	16.033	1.00	22.05
ATOM	92	CD2	LEU	202	4.459	24.159	17.554	1.00	23.90
ATOM	93	C	LEU	202	5.398	25.609	13.585	1.00	25.03
ATOM	94	O	LEU	202	6.563	25.645	13.962	1.00	26.19
ATOM	95	N	HIS	203	4.796	26.637	13.000	1.00	24.59
ATOM	96	CA	HIS	203	5.449	27.923	12.874	1.00	26.20
ATOM	97	CB	HIS	203	5.295	28.476	11.451	1.00	25.91
ATOM	98	CG	HIS	203	5.862	27.588	10.384	1.00	24.03
ATOM	99	CD2	HIS	203	5.581	27.497	9.062	1.00	24.35
ATOM	100	ND1	HIS	203	6.827	26.637	10.633	1.00	25.58
ATOM	101	CE1	HIS	203	7.115	25.994	9.517	1.00	23.23
ATOM	102	NE2	HIS	203	6.372	26.498	8.548	1.00	24.13
ATOM	103	C	HIS	203	4.763	28.836	13.877	1.00	28.92
ATOM	104	O	HIS	203	3.590	29.174	13.711	1.00	29.53
ATOM	105	N	ALA	204	5.479	29.191	14.939	1.00	30.12
ATOM	106	CA	ALA	204	4.936	30.043	15.982	1.00	30.61
ATOM	107	CB	ALA	204	4.275	29.193	17.066	1.00	30.68
ATOM	108	C	ALA	204	6.093	30.831	16.555	1.00	31.44
ATOM	109	O	ALA	204	7.201	30.310	16.662	1.00	32.23
ATOM	110	N	PRO	205	5.847	32.092	16.957	1.00	32.19
ATOM	111	CD	PRO	205	4.523	32.742	16.980	1.00	32.11

ATOM	112	CA	PRO	205	6.872	32.978	17.524	1.00	31.56
ATOM	113	CB	PRO	205	6.102	34.282	17.748	1.00	31.92
ATOM	114	CG	PRO	205	4.708	33.804	18.033	1.00	31.71
ATOM	115	C	PRO	205	7.525	32.474	18.805	1.00	30.91
ATOM	116	O	PRO	205	6.924	31.728	19.566	1.00	30.86
ATOM	117	N	THR	206	8.764	32.888	19.037	1.00	31.28
ATOM	118	CA	THR	206	9.492	32.486	20.228	1.00	32.05
ATOM	119	CB	THR	206	10.872	33.160	20.276	1.00	32.26
ATOM	120	OG1	THR	206	11.616	32.779	19.115	1.00	35.41
ATOM	121	CG2	THR	206	11.641	32.740	21.506	1.00	32.09
ATOM	122	C	THR	206	8.674	32.894	21.444	1.00	32.25
ATOM	123	O	THR	206	8.038	33.942	21.439	1.00	34.50
ATOM	124	N	GLY	207	8.664	32.052	22.470	1.00	31.86
ATOM	125	CA	GLY	207	7.894	32.358	23.661	1.00	31.13
ATOM	126	C	GLY	207	6.455	31.860	23.626	1.00	30.15
ATOM	127	O	GLY	207	5.765	31.891	24.642	1.00	31.27
ATOM	128	N	SER	208	6.005	31.362	22.480	1.00	29.48
ATOM	129	CA	SER	208	4.642	30.868	22.374	1.00	28.52
ATOM	130	CB	SER	208	4.182	30.872	20.908	1.00	27.20
ATOM	131	OG	SER	208	5.029	30.097	20.086	1.00	25.55
ATOM	132	C	SER	208	4.415	29.497	23.033	1.00	28.55
ATOM	133	O	SER	208	3.271	29.044	23.149	1.00	29.28
ATOM	134	N	GLY	209	5.494	28.840	23.463	1.00	28.23
ATOM	135	CA	GLY	209	5.367	27.540	24.120	1.00	28.17
ATOM	136	C	GLY	209	5.508	26.273	23.279	1.00	29.13
ATOM	137	O	GLY	209	5.108	25.181	23.721	1.00	27.88
ATOM	138	N	LYS	210	6.110	26.398	22.096	1.00	29.07
ATOM	139	CA	LYS	210	6.318	25.267	21.180	1.00	28.86
ATOM	140	CB	LYS	210	7.066	25.726	19.920	1.00	29.78
ATOM	141	CG	LYS	210	6.367	26.802	19.103	1.00	30.86
ATOM	142	CD	LYS	210	7.072	27.040	17.770	1.00	30.40
ATOM	143	CE	LYS	210	8.506	27.502	17.959	1.00	31.43
ATOM	144	NZ	LYS	210	8.607	28.803	18.689	1.00	33.79
ATOM	145	C	LYS	210	7.092	24.098	21.797	1.00	28.32
ATOM	146	O	LYS	210	6.829	22.935	21.498	1.00	28.11
ATOM	147	N	SER	211	8.072	24.411	22.630	1.00	28.62
ATOM	148	CA	SER	211	8.876	23.377	23.256	1.00	28.88
ATOM	149	CB	SER	211	10.348	23.763	23.172	1.00	30.34
ATOM	150	OG	SER	211	10.516	25.162	23.338	1.00	32.24
ATOM	151	C	SER	211	8.509	23.084	24.700	1.00	28.90
ATOM	152	O	SER	211	9.241	22.376	25.384	1.00	29.14
ATOM	153	N	THR	212	7.367	23.599	25.152	1.00	29.90
ATOM	154	CA	THR	212	6.925	23.399	26.532	1.00	29.80
ATOM	155	CB	THR	212	7.371	24.579	27.415	1.00	28.95
ATOM	156	OG1	THR	212	7.033	25.814	26.768	1.00	29.28
ATOM	157	CG2	THR	212	8.870	24.531	27.651	1.00	26.88
ATOM	158	C	THR	212	5.412	23.193	26.686	1.00	29.89
ATOM	159	O	THR	212	4.949	22.153	27.166	1.00	29.41
ATOM	160	N	LYS	213	4.641	24.191	26.277	1.00	31.79
ATOM	161	CA	LYS	213	3.135	24.128	26.374	1.00	31.17
ATOM	162	CB	LYS	213	2.576	25.486	26.013	1.00	31.92
ATOM	163	CG	LYS	213	1.066	25.565	26.123	1.00	33.79
ATOM	164	CD	LYS	213	0.627	27.019	26.126	1.00	36.61
ATOM	165	CE	LYS	213	-0.887	27.169	26.155	1.00	38.22
ATOM	166	NZ	LYS	213	-1.254	28.563	26.558	1.00	38.71
ATOM	167	C	LYS	213	2.636	23.043	25.464	1.00	30.15
ATOM	168	O	LYS	213	1.836	22.212	25.894	1.00	29.46
ATOM	169	N	VAL	214	3.110	23.026	24.222	1.00	29.37

ATOM	170	CA	VAL	214	2.657	22.042	23.247	1.00	29.35
ATOM	171	CB	VAL	214	3.274	22.317	21.845	1.00	30.43
ATOM	172	CG1	VAL	214	2.805	21.296	20.826	1.00	29.20
ATOM	173	CG2	VAL	214	2.881	23.719	21.381	1.00	31.27
ATOM	174	C	VAL	214	2.903	20.604	23.725	1.00	27.79
ATOM	175	O	VAL	214	1.980	19.781	23.722	1.00	29.24
ATOM	176	N	PRO	215	4.146	20.268	24.125	1.00	25.78
ATOM	177	CD	PRO	215	5.439	20.966	24.012	1.00	24.07
ATOM	178	CA	PRO	215	4.338	18.887	24.586	1.00	24.86
ATOM	179	CB	PRO	215	5.862	18.782	24.767	1.00	22.92
ATOM	180	CG	PRO	215	6.298	20.185	24.983	1.00	23.18
ATOM	181	C	PRO	215	3.556	18.590	25.878	1.00	23.85
ATOM	182	O	PRO	215	3.157	17.448	26.109	1.00	24.03
ATOM	183	N	ALA	216	3.322	19.615	26.700	1.00	24.13
ATOM	184	CA	ALA	216	2.555	19.466	27.946	1.00	24.64
ATOM	185	CB	ALA	216	2.592	20.754	28.741	1.00	23.09
ATOM	186	C	ALA	216	1.100	19.089	27.616	1.00	25.20
ATOM	187	O	ALA	216	0.517	18.192	28.232	1.00	25.36
ATOM	188	N	ALA	217	0.524	19.773	26.631	1.00	25.49
ATOM	189	CA	ALA	217	-0.836	19.501	26.187	1.00	25.40
ATOM	190	CB	ALA	217	-1.277	20.565	25.194	1.00	23.76
ATOM	191	C	ALA	217	-0.905	18.104	25.547	1.00	25.48
ATOM	192	O	ALA	217	-1.878	17.373	25.725	1.00	25.77
ATOM	193	N	TYR	218	0.136	17.735	24.807	1.00	25.42
ATOM	194	CA	TYR	218	0.191	16.422	24.165	1.00	24.86
ATOM	195	CB	TYR	218	1.410	16.306	23.243	1.00	24.75
ATOM	196	CG	TYR	218	1.253	16.946	21.882	1.00	24.58
ATOM	197	CD1	TYR	218	0.072	16.795	21.146	1.00	23.47
ATOM	198	CE1	TYR	218	-0.048	17.332	19.858	1.00	24.75
ATOM	199	CD2	TYR	218	2.310	17.656	21.303	1.00	23.47
ATOM	200	CE2	TYR	218	2.205	18.192	20.021	1.00	23.76
ATOM	201	CZ	TYR	218	1.025	18.028	19.299	1.00	25.01
ATOM	202	OH	TYR	218	0.924	18.553	18.023	1.00	24.22
ATOM	203	C	TYR	218	0.245	15.294	25.183	1.00	23.95
ATOM	204	O	TYR	218	-0.499	14.324	25.065	1.00	25.49
ATOM	205	N	ALA	219	1.140	15.410	26.160	1.00	23.90
ATOM	206	CA	ALA	219	1.305	14.388	27.204	1.00	25.10
ATOM	207	CB	ALA	219	2.553	14.673	28.033	1.00	23.15
ATOM	208	C	ALA	219	0.079	14.281	28.115	1.00	26.52
ATOM	209	O	ALA	219	-0.257	13.193	28.595	1.00	26.05
ATOM	210	N	ALA	220	-0.591	15.416	28.328	1.00	28.32
ATOM	211	CA	ALA	220	-1.789	15.484	29.161	1.00	27.69
ATOM	212	CB	ALA	220	-2.224	16.933	29.346	1.00	28.77
ATOM	213	C	ALA	220	-2.904	14.666	28.528	1.00	27.42
ATOM	214	O	ALA	220	-3.873	14.315	29.190	1.00	27.84
ATOM	215	N	GLN	221	-2.762	14.380	27.236	1.00	28.01
ATOM	216	CA	GLN	221	-3.733	13.576	26.492	1.00	27.15
ATOM	217	CB	GLN	221	-3.782	13.991	25.027	1.00	28.76
ATOM	218	CG	GLN	221	-4.413	15.331	24.739	1.00	30.06
ATOM	219	CD	GLN	221	-4.084	15.798	23.335	1.00	32.54
ATOM	220	OE1	GLN	221	-4.457	15.159	22.346	1.00	34.37
ATOM	221	NE2	GLN	221	-3.350	16.895	23.238	1.00	34.38
ATOM	222	C	GLN	221	-3.321	12.119	26.554	1.00	26.58
ATOM	223	O	GLN	221	-3.881	11.284	25.851	1.00	27.44
ATOM	224	N	GLY	222	-2.285	11.833	27.334	1.00	25.93
ATOM	225	CA	GLY	222	-1.828	10.472	27.487	1.00	24.98
ATOM	226	C	GLY	222	-0.767	9.987	26.530	1.00	26.33
ATOM	227	O	GLY	222	-0.561	8.733	26.414	1.00	27.70

ATOM	228	N	TYR	223	-0.057	10.896	25.875	1.00	26.89
ATOM	229	CA	TYR	223	0.995	10.498	24.940	1.00	25.87
ATOM	230	CB	TYR	223	0.901	11.316	23.665	1.00	25.29
ATOM	231	CG	TYR	223	-0.373	11.111	22.906	1.00	25.96
ATOM	232	CD1	TYR	223	-1.399	12.045	22.974	1.00	25.65
ATOM	233	CE1	TYR	223	-2.559	11.873	22.250	1.00	27.75
ATOM	234	CD2	TYR	223	-0.542	9.993	22.096	1.00	26.27
ATOM	235	CE2	TYR	223	-1.692	9.808	21.372	1.00	27.03
ATOM	236	CZ	TYR	223	-2.698	10.749	21.446	1.00	28.75
ATOM	237	OH	TYR	223	-3.839	10.573	20.695	1.00	32.89
ATOM	238	C	TYR	223	2.415	10.629	25.483	1.00	26.22
ATOM	239	O	TYR	223	2.697	11.441	26.373	1.00	25.06
ATOM	240	N	LYS	224	3.308	9.826	24.919	1.00	27.21
ATOM	241	CA	LYS	224	4.721	9.850	25.270	1.00	27.71
ATOM	242	CB	LYS	224	5.325	8.460	25.107	1.00	29.76
ATOM	243	CG	LYS	224	4.827	7.470	26.139	1.00	35.42
ATOM	244	CD	LYS	224	5.314	7.887	27.525	1.00	39.88
ATOM	245	CE	LYS	224	4.771	7.005	28.652	1.00	41.50
ATOM	246	NZ	LYS	224	5.385	7.396	29.969	1.00	42.40
ATOM	247	C	LYS	224	5.309	10.821	24.258	1.00	26.68
ATOM	248	O	LYS	224	5.265	10.571	23.047	1.00	27.78
ATOM	249	N	VAL	225	5.785	11.959	24.746	1.00	25.81
ATOM	250	CA	VAL	225	6.333	12.998	23.883	1.00	24.37
ATOM	251	CB	VAL	225	5.649	14.354	24.161	1.00	24.83
ATOM	252	CG1	VAL	225	5.997	15.359	23.075	1.00	23.06
ATOM	253	CG2	VAL	225	4.137	14.166	24.274	1.00	25.36
ATOM	254	C	VAL	225	7.834	13.190	24.046	1.00	23.03
ATOM	255	O	VAL	225	8.355	13.220	25.166	1.00	20.40
ATOM	256	N	LEU	226	8.513	13.330	22.914	1.00	22.55
ATOM	257	CA	LEU	226	9.954	13.551	22.878	1.00	21.32
ATOM	258	CB	LEU	226	10.627	12.471	22.037	1.00	18.45
ATOM	259	CG	LEU	226	12.082	12.710	21.656	1.00	18.51
ATOM	260	CD1	LEU	226	12.985	12.577	22.884	1.00	16.54
ATOM	261	CD2	LEU	226	12.473	11.717	20.570	1.00	19.37
ATOM	262	C	LEU	226	10.192	14.926	22.253	1.00	20.71
ATOM	263	O	LEU	226	9.629	15.245	21.202	1.00	20.63
ATOM	264	N	VAL	227	10.993	15.752	22.912	1.00	22.06
ATOM	265	CA	VAL	227	11.290	17.087	22.404	1.00	22.02
ATOM	266	CB	VAL	227	10.915	18.173	23.425	1.00	20.33
ATOM	267	CG1	VAL	227	10.933	19.532	22.757	1.00	19.96
ATOM	268	CG2	VAL	227	9.561	17.881	24.043	1.00	19.10
ATOM	269	C	VAL	227	12.787	17.165	22.111	1.00	22.26
ATOM	270	O	VAL	227	13.612	17.040	23.023	1.00	23.12
ATOM	271	N	LEU	228	13.135	17.322	20.839	1.00	21.87
ATOM	272	CA	LEU	228	14.534	17.397	20.435	1.00	21.87
ATOM	273	CB	LEU	228	14.770	16.590	19.162	1.00	20.02
ATOM	274	CG	LEU	228	14.576	15.079	19.254	1.00	18.46
ATOM	275	CD1	LEU	228	14.817	14.488	17.874	1.00	17.50
ATOM	276	CD2	LEU	228	15.522	14.477	20.304	1.00	15.84
ATOM	277	C	LEU	228	14.961	18.833	20.216	1.00	22.19
ATOM	278	O	LEU	228	14.338	19.566	19.450	1.00	23.01
ATOM	279	N	ASN	229	16.063	19.211	20.849	1.00	22.54
ATOM	280	CA	ASN	229	16.587	20.567	20.756	1.00	22.64
ATOM	281	CB	ASN	229	16.276	21.301	22.067	1.00	23.81
ATOM	282	CG	ASN	229	16.582	22.770	22.008	1.00	24.90
ATOM	283	OD1	ASN	229	17.732	23.196	22.184	1.00	26.02
ATOM	284	ND2	ASN	229	15.548	23.568	21.794	1.00	24.10
ATOM	285	C	ASN	229	18.101	20.432	20.517	1.00	22.19

ATOM	286	O	ASN	229	18.756	19.525	20.938	1.00	19.92
ATOM	287	N	PRO	230	18.659	21.429	19.753	1.00	23.12
ATOM	288	CD	PRO	230	17.987	22.400	18.872	1.00	21.71
ATOM	289	CA	PRO	230	20.107	21.397	19.495	1.00	23.95
ATOM	290	CB	PRO	230	20.269	22.383	18.336	1.00	23.83
ATOM	291	CG	PRO	230	19.114	23.319	18.510	1.00	23.76
ATOM	292	C	PRO	230	21.011	21.755	20.688	1.00	24.47
ATOM	293	O	PRO	230	22.114	21.211	20.834	1.00	25.45
ATOM	294	N	SER	231	20.512	22.595	21.584	1.00	24.28
ATOM	295	CA	SER	231	21.290	23.036	22.727	1.00	24.31
ATOM	296	CB	SER	231	20.886	24.461	23.088	1.00	23.88
ATOM	297	OG	SER	231	21.566	24.896	24.251	1.00	27.81
ATOM	298	C	SER	231	21.236	22.165	23.975	1.00	25.03
ATOM	299	O	SER	231	20.157	21.870	24.496	1.00	25.25
ATOM	300	N	VAL	232	22.413	21.805	24.480	1.00	24.64
ATOM	301	CA	VAL	232	22.525	21.011	25.694	1.00	24.77
ATOM	302	CB	VAL	232	24.006	20.628	25.975	1.00	24.98
ATOM	303	CG1	VAL	232	24.184	20.163	27.417	1.00	24.08
ATOM	304	CG2	VAL	232	24.458	19.534	25.019	1.00	20.75
ATOM	305	C	VAL	232	21.976	21.862	26.852	1.00	26.64
ATOM	306	O	VAL	232	21.174	21.394	27.668	1.00	28.40
ATOM	307	N	ALA	233	22.365	23.133	26.879	1.00	26.57
ATOM	308	CA	ALA	233	21.916	24.051	27.922	1.00	26.13
ATOM	309	CB	ALA	233	22.592	25.417	27.759	1.00	25.46
ATOM	310	C	ALA	233	20.401	24.203	27.907	1.00	25.51
ATOM	311	O	ALA	233	19.764	24.124	28.952	1.00	26.22
ATOM	312	N	ALA	234	19.831	24.397	26.718	1.00	25.47
ATOM	313	CA	ALA	234	18.385	24.553	26.567	1.00	24.61
ATOM	314	CB	ALA	234	18.031	24.857	25.138	1.00	23.89
ATOM	315	C	ALA	234	17.653	23.304	27.015	1.00	25.81
ATOM	316	O	ALA	234	16.652	23.393	27.728	1.00	25.42
ATOM	317	N	THR	235	18.157	22.144	26.591	1.00	26.43
ATOM	318	CA	THR	235	17.556	20.868	26.951	1.00	26.97
ATOM	319	CB	THR	235	18.339	19.673	26.345	1.00	27.79
ATOM	320	OG1	THR	235	18.322	19.768	24.916	1.00	27.58
ATOM	321	CG2	THR	235	17.704	18.343	26.748	1.00	26.60
ATOM	322	C	THR	235	17.499	20.746	28.472	1.00	27.43
ATOM	323	O	THR	235	16.440	20.488	29.035	1.00	28.23
ATOM	324	N	LEU	236	18.624	20.984	29.138	1.00	27.19
ATOM	325	CA	LEU	236	18.670	20.898	30.595	1.00	27.35
ATOM	326	CB	LEU	236	20.086	21.185	31.096	1.00	28.04
ATOM	327	CG	LEU	236	21.174	20.151	30.842	1.00	27.41
ATOM	328	CD1	LEU	236	22.519	20.838	30.894	1.00	28.18
ATOM	329	CD2	LEU	236	21.086	19.028	31.858	1.00	26.49
ATOM	330	C	LEU	236	17.715	21.898	31.235	1.00	26.83
ATOM	331	O	LEU	236	17.054	21.601	32.232	1.00	27.18
ATOM	332	N	GLY	237	17.651	23.086	30.648	1.00	26.16
ATOM	333	CA	GLY	237	16.804	24.131	31.178	1.00	26.03
ATOM	334	C	GLY	237	15.333	23.812	31.228	1.00	25.39
ATOM	335	O	GLY	237	14.651	24.230	32.151	1.00	25.99
ATOM	336	N	PHE	238	14.841	23.065	30.252	1.00	25.78
ATOM	337	CA	PHE	238	13.428	22.721	30.205	1.00	27.27
ATOM	338	CB	PHE	238	13.138	21.811	29.013	1.00	27.38
ATOM	339	CG	PHE	238	13.274	22.495	27.691	1.00	29.37
ATOM	340	CD1	PHE	238	12.493	23.610	27.388	1.00	29.67
ATOM	341	CD2	PHE	238	14.202	22.352	26.756	1.00	29.17
ATOM	342	CE1	PHE	238	12.641	24.273	26.169	1.00	29.22
ATOM	343	CE2	PHE	238	14.354	22.707	25.541	1.00	28.63

ATOM	344	CZ	PHE	238	13.571	23.822	25.248	1.00	27.73
ATOM	345	C	PHE	238	12.908	22.087	31.488	1.00	28.44
ATOM	346	O	PHE	238	11.740	22.267	31.838	1.00	28.75
ATOM	347	N	GLY	239	13.782	21.377	32.199	1.00	29.43
ATOM	348	CA	GLY	239	13.387	20.728	33.439	1.00	30.17
ATOM	349	C	GLY	239	12.724	21.653	34.447	1.00	30.46
ATOM	350	O	GLY	239	11.590	21.420	34.874	1.00	30.46
ATOM	351	N	ALA	240	13.429	22.711	34.825	1.00	30.54
ATOM	352	CA	ALA	240	12.904	23.667	35.785	1.00	31.68
ATOM	353	CB	ALA	240	14.007	24.611	36.258	1.00	30.45
ATOM	354	C	ALA	240	11.732	24.460	35.216	1.00	31.56
ATOM	355	O	ALA	240	10.736	24.673	35.904	1.00	32.32
ATOM	356	N	TYR	241	11.836	24.873	33.957	1.00	31.75
ATOM	357	CA	TYR	241	10.770	25.653	33.340	1.00	30.92
ATOM	358	CB	TYR	241	11.139	26.095	31.920	1.00	31.44
ATOM	359	CG	TYR	241	10.037	26.903	31.250	1.00	33.57
ATOM	360	CD1	TYR	241	10.086	28.294	31.220	1.00	35.11
ATOM	361	CE1	TYR	241	9.052	29.038	30.657	1.00	36.03
ATOM	362	CD2	TYR	241	8.919	26.276	30.690	1.00	33.41
ATOM	363	CE2	TYR	241	7.889	27.006	30.133	1.00	34.12
ATOM	364	CZ	TYR	241	7.958	28.384	30.122	1.00	36.46
ATOM	365	OH	TYR	241	6.915	29.107	29.601	1.00	39.06
ATOM	366	C	TYR	241	9.464	24.885	33.288	1.00	29.43
ATOM	367	O	TYR	241	8.402	25.452	33.500	1.00	28.88
ATOM	368	N	MET	242	9.547	23.613	32.932	1.00	28.93
ATOM	369	CA	MET	242	8.368	22.767	32.824	1.00	29.09
ATOM	370	CB	MET	242	8.735	21.464	32.106	1.00	28.71
ATOM	371	CG	MET	242	8.956	21.646	30.602	1.00	27.19
ATOM	372	SD	MET	242	7.445	22.198	29.767	1.00	24.74
ATOM	373	CE	MET	242	6.543	20.617	29.574	1.00	25.21
ATOM	374	C	MET	242	7.732	22.501	34.191	1.00	28.87
ATOM	375	O	MET	242	6.507	22.451	34.339	1.00	25.61
ATOM	376	N	SER	243	8.581	22.366	35.195	1.00	31.13
ATOM	377	CA	SER	243	8.125	22.137	36.543	1.00	31.64
ATOM	378	CB	SER	243	9.325	21.864	37.445	1.00	32.82
ATOM	379	OG	SER	243	8.916	21.422	38.725	1.00	37.37
ATOM	380	C	SER	243	7.378	23.390	36.994	1.00	31.87
ATOM	381	O	SER	243	6.226	23.320	37.420	1.00	32.45
ATOM	382	N	ALA	244	8.000	24.547	36.806	1.00	31.20
ATOM	383	CA	ALA	244	7.387	25.806	37.218	1.00	30.80
ATOM	384	CB	ALA	244	8.414	26.947	37.163	1.00	30.58
ATOM	385	C	ALA	244	6.148	26.182	36.420	1.00	29.56
ATOM	386	O	ALA	244	5.144	26.608	36.985	1.00	30.91
ATOM	387	N	ALA	245	6.205	25.994	35.113	1.00	27.79
ATOM	388	CA	ALA	245	5.093	26.369	34.261	1.00	27.16
ATOM	389	CB	ALA	245	5.601	26.694	32.871	1.00	26.05
ATOM	390	C	ALA	245	3.966	25.363	34.171	1.00	27.41
ATOM	391	O	ALA	245	2.804	25.742	34.001	1.00	27.65
ATOM	392	N	HIS	246	4.295	24.083	34.278	1.00	27.72
ATOM	393	CA	HIS	246	3.230	23.050	34.134	1.00	26.52
ATOM	394	CB	HIS	246	3.437	22.414	32.751	1.00	26.99
ATOM	395	CG	HIS	246	3.348	23.395	31.626	1.00	24.43
ATOM	396	CD2	HIS	246	4.309	23.992	30.882	1.00	26.07
ATOM	397	ND1	HIS	246	2.147	23.335	31.161	1.00	26.33
ATOM	398	CE1	HIS	246	2.369	24.741	30.179	1.00	25.34
ATOM	399	NE2	HIS	246	3.673	24.835	29.991	1.00	26.40
ATOM	400	C	HIS	246	3.245	21.961	35.208	1.00	26.80
ATOM	401	O	HIS	246	2.445	21.035	35.119	1.00	25.51

ATOM	402	N	GLY	247	4.097	22.073	36.223	1.00	26.76
ATOM	403	CA	GLY	247	4.123	21.069	37.267	1.00	26.09
ATOM	404	C	GLY	247	4.509	19.740	36.657	1.00	27.58
ATOM	405	O	GLY	247	3.899	18.701	36.945	1.00	28.05
ATOM	406	N	VAL	248	5.497	19.782	35.768	1.00	27.72
ATOM	407	CA	VAL	248	5.985	18.589	35.088	1.00	27.72
ATOM	408	CB	VAL	248	5.712	18.668	33.558	1.00	28.05
ATOM	409	CG1	VAL	248	6.274	17.450	32.854	1.00	28.78
ATOM	410	CG2	VAL	248	4.220	18.792	33.278	1.00	27.03
ATOM	411	C	VAL	248	7.488	18.441	35.307	1.00	27.70
ATOM	412	O	VAL	248	8.229	19.414	35.224	1.00	27.56
ATOM	413	N	ASP	249	7.923	17.228	35.622	1.00	29.51
ATOM	414	CA	ASP	249	9.342	16.928	35.813	1.00	31.97
ATOM	415	CB	ASP	249	9.563	16.290	37.187	1.00	36.65
ATOM	416	CG	ASP	249	8.834	17.029	38.296	1.00	42.98
ATOM	417	OD1	ASP	249	9.183	18.198	38.578	1.00	48.26
ATOM	418	OD2	ASP	249	7.897	16.448	38.884	1.00	47.15
ATOM	419	C	ASP	249	9.655	15.927	34.697	1.00	30.40
ATOM	420	O	ASP	249	9.444	14.721	34.854	1.00	32.54
ATOM	421	N	PRO	250	10.112	16.412	33.531	1.00	28.60
ATOM	422	CD	PRO	250	10.397	17.809	33.145	1.00	28.10
ATOM	423	CA	PRO	250	10.411	15.500	32.424	1.00	27.32
ATOM	424	CB	PRO	250	10.356	16.432	31.218	1.00	25.82
ATOM	425	CG	PRO	250	10.998	17.658	31.748	1.00	25.77
ATOM	426	C	PRO	250	11.756	14.787	32.504	1.00	27.35
ATOM	427	O	PRO	250	12.581	15.083	33.368	1.00	27.56
ATOM	428	N	ASN	251	11.944	13.805	31.629	1.00	27.78
ATOM	429	CA	ASN	251	13.213	13.090	31.553	1.00	27.99
ATOM	430	CB	ASN	251	13.046	11.776	30.802	1.00	27.88
ATOM	431	CG	ASN	251	11.944	10.914	31.380	1.00	29.52
ATOM	432	OD1	ASN	251	12.136	10.211	32.377	1.00	29.08
ATOM	433	ND2	ASN	251	10.770	10.978	30.768	1.00	30.24
ATOM	434	C	ASN	251	14.131	14.026	30.763	1.00	28.29
ATOM	435	O	ASN	251	13.687	14.685	29.808	1.00	27.76
ATOM	436	N	ILE	252	15.387	14.131	31.185	1.00	28.26
ATOM	437	CA	ILE	252	16.349	15.004	30.517	1.00	27.72
ATOM	438	CB	ILE	252	16.891	16.081	31.491	1.00	25.56
ATOM	439	CG2	ILE	252	17.909	16.978	30.780	1.00	24.45
ATOM	440	CG1	ILE	252	15.731	16.880	32.116	1.00	23.07
ATOM	441	CD1	ILE	252	14.946	17.753	31.147	1.00	20.19
ATOM	442	C	ILE	252	17.511	14.157	29.995	1.00	29.20
ATOM	443	O	ILE	252	18.148	13.435	30.759	1.00	29.28
ATOM	444	N	ARG	253	17.776	14.230	28.695	1.00	29.57
ATOM	445	CA	ARG	253	18.862	13.455	28.109	1.00	29.87
ATOM	446	CB	ARG	253	18.306	12.366	27.207	1.00	30.75
ATOM	447	CG	ARG	253	17.023	11.733	27.695	1.00	32.49
ATOM	448	CD	ARG	253	16.943	10.331	27.175	1.00	35.54
ATOM	449	NE	ARG	253	18.046	9.553	27.726	1.00	40.71
ATOM	450	CZ	ARG	253	18.431	8.369	27.272	1.00	41.75
ATOM	451	NH1	ARG	253	19.449	7.743	27.846	1.00	42.45
ATOM	452	NH2	ARG	253	17.814	7.822	26.233	1.00	44.21
ATOM	453	C	ARG	253	19.858	14.296	27.309	1.00	31.31
ATOM	454	O	ARG	253	19.547	14.791	26.218	1.00	30.51
ATOM	455	N	THR	254	21.046	14.434	27.876	1.00	32.71
ATOM	456	CA	THR	254	22.114	15.225	27.214	1.00	33.25
ATOM	457	CB	THR	254	22.386	16.599	27.876	1.00	31.25
ATOM	458	CG1	THR	254	22.880	16.414	29.206	1.00	29.55
ATOM	459	CG2	THR	254	21.113	17.427	27.921	1.00	30.34

ATOM	460	C	THR	254	23.374	14.370	27.289	1.00	35.29
ATOM	461	O	THR	254	23.378	13.313	27.926	1.00	34.39
ATOM	462	N	GLY	255	24.435	14.818	26.625	1.00	37.19
ATOM	463	CA	GLY	255	25.680	14.075	26.656	1.00	38.93
ATOM	464	C	GLY	255	26.217	14.023	28.072	1.00	40.31
ATOM	465	O	GLY	255	26.605	12.963	28.566	1.00	40.42
ATOM	466	N	VAL	256	26.192	15.169	28.744	1.00	41.59
ATOM	467	CA	VAL	256	26.684	15.252	30.111	1.00	43.59
ATOM	468	CB	VAL	256	26.869	16.712	30.597	1.00	43.46
ATOM	469	CG1	VAL	256	28.182	17.268	30.084	1.00	46.24
ATOM	470	CG2	VAL	256	25.705	17.591	30.153	1.00	43.43
ATOM	471	C	VAL	256	25.839	14.516	31.137	1.00	44.62
ATOM	472	O	VAL	256	26.356	13.667	31.860	1.00	45.65
ATOM	473	N	ARG	257	24.540	14.810	31.172	1.00	45.28
ATOM	474	CA	ARG	257	23.651	14.203	32.156	1.00	44.14
ATOM	475	CB	ARG	257	23.445	15.197	33.311	1.00	45.53
ATOM	476	CG	ARG	257	22.434	14.762	34.357	1.00	49.87
ATOM	477	CD	ARG	257	22.485	15.627	35.618	1.00	52.65
ATOM	478	NE	ARG	257	21.615	15.118	36.686	1.00	56.84
ATOM	479	CZ	ARG	257	21.608	13.858	37.140	1.00	58.71
ATOM	480	NH1	ARG	257	22.424	12.935	36.632	1.00	58.53
ATOM	481	NH2	ARG	257	20.778	13.513	38.119	1.00	59.13
ATOM	482	C	ARG	257	22.291	13.718	31.654	1.00	42.81
ATOM	483	O	ARG	257	21.629	14.385	30.856	1.00	42.13
ATOM	484	N	THR	258	21.896	12.544	32.136	1.00	42.22
ATOM	485	CA	THR	258	20.601	11.949	31.834	1.00	41.75
ATOM	486	CB	THR	258	20.730	10.521	31.268	1.00	41.55
ATOM	487	OG1	THR	258	21.112	10.588	29.890	1.00	43.65
ATOM	488	CG2	THR	258	19.411	9.770	31.376	1.00	41.26
ATOM	489	C	THR	258	19.864	11.902	33.173	1.00	41.88
ATOM	490	O	THR	258	20.431	11.489	34.191	1.00	43.37
ATOM	491	N	ILE	259	18.635	12.398	33.184	1.00	40.14
ATOM	492	CA	ILE	259	17.815	12.424	34.382	1.00	38.42
ATOM	493	CB	ILE	259	17.506	13.870	34.799	1.00	37.89
ATOM	494	CG2	ILE	259	16.631	13.891	36.043	1.00	38.14
ATOM	495	CG1	ILE	259	18.805	14.649	35.011	1.00	37.37
ATOM	496	CD1	ILE	259	18.593	16.115	35.332	1.00	37.01
ATOM	497	C	ILE	259	16.516	11.736	33.998	1.00	38.66
ATOM	498	O	ILE	259	15.754	12.258	33.185	1.00	38.35
ATOM	499	N	THR	260	16.307	10.532	34.510	1.00	39.27
ATOM	500	CA	THR	260	15.090	9.790	34.208	1.00	40.28
ATOM	501	CB	THR	260	15.384	8.297	33.979	1.00	41.32
ATOM	502	OG1	THR	260	16.401	8.165	32.977	1.00	42.58
ATOM	503	CG2	THR	260	14.125	7.573	33.504	1.00	42.71
ATOM	504	C	THR	260	14.075	9.989	35.333	1.00	39.99
ATOM	505	O	THR	260	14.356	9.733	36.504	1.00	39.99
ATOM	506	N	THR	261	12.894	10.452	34.958	1.00	39.53
ATOM	507	CA	THR	261	11.842	10.740	35.910	1.00	39.43
ATOM	508	CB	THR	261	11.392	12.185	35.717	1.00	40.25
ATOM	509	OG1	THR	261	12.527	13.049	35.864	1.00	42.32
ATOM	510	CG2	THR	261	10.337	12.562	36.723	1.00	42.64
ATOM	511	C	THR	261	10.628	9.829	35.793	1.00	38.62
ATOM	512	O	THR	261	9.843	9.700	36.736	1.00	39.27
ATOM	513	N	GLY	262	10.476	9.177	34.648	1.00	36.63
ATOM	514	CA	GLY	262	9.316	8.323	34.462	1.00	34.27
ATOM	515	C	GLY	262	8.185	9.149	33.875	1.00	32.70
ATOM	516	O	GLY	262	7.037	8.708	33.802	1.00	32.40
ATOM	517	N	SER	263	8.528	10.368	33.464	1.00	30.97

ATOM	518	CA	SER	263	7.571	11.282	32.861	1.00	28.52
ATOM	519	CB	SER	263	8.148	12.705	32.871	1.00	27.84
ATOM	520	OG	SER	263	7.276	13.641	32.251	1.00	26.21
ATOM	521	C	SER	263	7.286	10.852	31.420	1.00	27.13
ATOM	522	O	SER	263	8.092	10.151	30.796	1.00	25.11
ATOM	523	N	PRO	264	6.091	11.189	30.907	1.00	25.91
ATOM	524	CD	PRO	264	4.919	11.756	31.593	1.00	24.44
ATOM	525	CA	PRO	264	5.757	10.825	29.528	1.00	25.37
ATOM	526	CB	PRO	264	4.252	11.072	29.466	1.00	24.70
ATOM	527	CG	PRO	264	4.059	12.176	30.433	1.00	25.43
ATOM	528	C	PRO	264	6.516	11.761	28.575	1.00	25.19
ATOM	529	O	PRO	264	6.637	11.488	27.378	1.00	24.68
ATOM	530	N	ILE	265	7.009	12.874	29.113	1.00	25.11
ATOM	531	CA	ILE	265	7.760	13.839	28.323	1.00	24.64
ATOM	532	CB	ILE	265	7.395	15.284	28.689	1.00	24.85
ATOM	533	CG2	ILE	265	8.045	16.250	27.706	1.00	24.63
ATOM	534	CG1	ILE	265	5.880	15.463	28.623	1.00	25.72
ATOM	535	CD1	ILE	265	5.398	16.810	29.116	1.00	27.30
ATOM	536	C	ILE	265	9.257	13.646	28.498	1.00	23.56
ATOM	537	O	ILE	265	9.756	13.474	29.612	1.00	23.63
ATOM	538	N	THR	266	9.974	13.683	27.386	1.00	23.74
ATOM	539	CA	THR	266	11.419	13.510	27.391	1.00	22.48
ATOM	540	CB	THR	266	11.799	12.115	26.833	1.00	21.23
ATOM	541	OG1	THR	266	11.288	11.107	27.707	1.00	20.89
ATOM	542	CG2	THR	266	13.295	11.952	26.716	1.00	21.86
ATOM	543	C	THR	266	12.060	14.585	26.530	1.00	21.76
ATOM	544	O	THR	266	11.674	14.770	25.376	1.00	20.29
ATOM	545	N	TYR	267	12.981	15.341	27.119	1.00	21.86
ATOM	546	CA	TYR	267	13.702	16.372	26.388	1.00	22.28
ATOM	547	CB	TYR	267	13.833	17.654	27.211	1.00	22.75
ATOM	548	CG	TYR	267	12.563	18.464	27.278	1.00	24.36
ATOM	549	CD1	TYR	267	11.666	18.297	28.327	1.00	22.30
ATOM	550	CE1	TYR	267	10.493	19.034	28.386	1.00	22.80
ATOM	551	CD2	TYR	267	12.253	19.396	26.281	1.00	23.66
ATOM	552	CE2	TYR	267	11.080	20.139	26.332	1.00	24.13
ATOM	553	CZ	TYR	267	10.206	19.949	27.391	1.00	23.99
ATOM	554	OH	TYR	267	9.045	20.674	27.465	1.00	23.95
ATOM	555	C	TYR	267	15.078	15.805	26.108	1.00	22.43
ATOM	556	O	TYR	267	15.679	15.165	26.978	1.00	23.25
ATOM	557	N	SER	268	15.573	16.031	24.900	1.00	22.28
ATOM	558	CA	SER	268	16.884	15.532	24.512	1.00	22.21
ATOM	559	CB	SER	268	16.750	14.082	24.010	1.00	22.96
ATOM	560	OG	SER	268	17.948	13.556	23.441	1.00	19.87
ATOM	561	C	SER	268	17.484	16.401	23.419	1.00	22.55
ATOM	562	O	SER	268	16.774	17.111	22.706	1.00	23.40
ATOM	563	N	THR	269	18.809	16.391	23.348	1.00	23.70
ATOM	564	CA	THR	269	19.547	17.102	22.310	1.00	22.50
ATOM	565	CB	THR	269	21.031	17.245	22.694	1.00	22.70
ATOM	566	OG1	THR	269	21.510	15.986	23.193	1.00	19.49
ATOM	567	CG2	THR	269	21.218	18.313	23.744	1.00	20.70
ATOM	568	C	THR	269	19.495	16.149	21.110	1.00	22.45
ATOM	569	O	THR	269	19.222	14.950	21.269	1.00	22.71
ATOM	570	N	TYR	270	19.746	16.656	19.910	1.00	22.86
ATOM	571	CA	TYR	270	19.746	15.777	18.747	1.00	22.07
ATOM	572	CB	TYR	270	19.312	16.591	17.446	1.00	20.62
ATOM	573	CG	TYR	270	18.535	17.330	17.123	1.00	19.62
ATOM	574	CD1	TYR	270	18.392	18.677	17.452	1.00	20.22
ATOM	575	CE1	TYR	270	17.242	19.339	17.118	1.00	18.99

ATOM	576	CD2	TYR	270	17.488	16.704	16.454	1.00	18.83
ATOM	577	CE2	TYR	270	16.331	17.406	16.115	1.00	20.81
ATOM	578	CZ	TYR	270	16.218	18.752	16.451	1.00	20.32
ATOM	579	OH	TYR	270	15.086	19.457	16.112	1.00	18.84
ATOM	580	C	TYR	270	20.943	14.828	18.852	1.00	21.56
ATOM	581	O	TYR	270	20.850	13.654	18.486	1.00	23.69
ATOM	582	N	GLY	271	22.043	15.333	19.406	1.00	19.54
ATOM	583	CA	GLY	271	23.242	14.534	19.555	1.00	19.07
ATOM	584	C	GLY	271	23.012	13.299	20.394	1.00	19.18
ATOM	585	O	GLY	271	23.330	12.192	19.980	1.00	19.27
ATOM	586	N	LYS	272	22.494	13.499	21.600	1.00	21.00
ATOM	587	CA	LYS	272	22.209	12.399	22.516	1.00	22.97
ATOM	588	CB	LYS	272	21.709	12.968	23.850	1.00	24.05
ATOM	589	CG	LYS	272	21.538	11.960	24.963	1.00	26.57
ATOM	590	CD	LYS	272	22.761	11.085	25.118	1.00	28.96
ATOM	591	CE	LYS	272	22.573	10.081	26.243	1.00	30.16
ATOM	592	NZ	LYS	272	23.623	9.033	26.198	1.00	31.88
ATOM	593	C	LYS	272	21.187	11.424	21.885	1.00	23.97
ATOM	594	O	LYS	272	21.351	10.198	21.964	1.00	24.73
ATOM	595	N	PHE	273	20.173	11.967	21.204	1.00	23.94
ATOM	596	CA	PHE	273	19.151	11.153	20.538	1.00	22.60
ATOM	597	CB	PHE	273	18.170	12.068	19.790	1.00	20.76
ATOM	598	CG	PHE	273	17.188	11.333	18.917	1.00	19.28
ATOM	599	CD1	PHE	273	16.138	10.611	19.476	1.00	19.37
ATOM	600	CD2	PHE	273	17.299	11.382	17.536	1.00	17.87
ATOM	601	CE1	PHE	273	15.211	9.951	18.670	1.00	18.22
ATOM	602	CE2	PHE	273	16.382	10.727	16.724	1.00	19.02
ATOM	603	CZ	PHE	273	15.334	10.010	17.293	1.00	17.46
ATOM	604	C	PHE	273	19.840	10.191	19.561	1.00	21.90
ATOM	605	O	PHE	273	19.619	8.970	19.580	1.00	20.97
ATOM	606	N	LEU	274	20.685	10.766	18.712	1.00	22.63
ATOM	607	CA	LEU	274	21.455	10.020	17.726	1.00	21.66
ATOM	608	CB	LEU	274	22.324	10.989	16.921	1.00	21.04
ATOM	609	CG	LEU	274	21.624	11.852	15.874	1.00	18.37
ATOM	610	CD1	LEU	274	22.546	12.969	15.437	1.00	16.98
ATOM	611	CD2	LEU	274	21.233	10.972	14.697	1.00	16.49
ATOM	612	C	LEU	274	22.346	8.971	18.403	1.00	21.93
ATOM	613	O	LEU	274	22.503	7.853	17.903	1.00	19.56
ATOM	614	N	ALA	275	22.944	9.362	19.525	1.00	23.03
ATOM	615	CA	ALA	275	23.818	8.493	20.300	1.00	24.57
ATOM	616	CB	ALA	275	24.585	9.301	21.322	1.00	21.93
ATOM	617	C	ALA	275	23.033	7.381	20.992	1.00	26.77
ATOM	618	O	ALA	275	23.580	6.302	21.237	1.00	28.37
ATOM	619	N	ASP	276	21.764	7.631	21.314	1.00	27.59
ATOM	620	CA	ASP	276	20.952	6.604	21.968	1.00	28.62
ATOM	621	CB	ASP	276	19.859	7.225	22.847	1.00	28.88
ATOM	622	CG	ASP	276	20.412	7.872	24.107	1.00	28.41
ATOM	623	OD1	ASP	276	21.515	7.500	24.553	1.00	28.79
ATOM	624	OD2	ASP	276	19.741	8.767	24.649	1.00	29.37
ATOM	625	C	ASP	276	20.350	5.614	20.971	1.00	29.04
ATOM	626	O	ASP	276	19.589	4.719	21.346	1.00	30.14
ATOM	627	N	GLY	277	20.700	5.775	19.701	1.00	29.48
ATOM	628	CA	GLY	277	20.201	4.876	18.677	1.00	29.32
ATOM	629	C	GLY	277	18.987	5.363	17.904	1.00	30.36
ATOM	630	O	GLY	277	18.343	4.574	17.211	1.00	31.50
ATOM	631	N	GLY	278	18.667	6.650	17.997	1.00	30.29
ATOM	632	CA	GLY	278	17.517	7.152	17.269	1.00	29.28
ATOM	633	C	GLY	278	16.193	6.655	17.827	1.00	28.53

ATOM	634	O	GLY	278	16.005	6.611	19.037	1.00	28.84
ATOM	635	N	CME	279	15.279	6.255	16.956	1.00	27.25
ATOM	636	CA	CME	279	13.973	5.792	17.394	1.00	28.61
ATOM	637	C	CME	279	13.976	4.530	18.265	1.00	30.15
ATOM	638	O	CME	279	13.004	4.243	18.959	1.00	31.77
ATOM	639	CB	CME	279	13.043	5.619	16.190	1.00	27.21
ATOM	640	SG	CME	279	12.348	7.190	15.561	1.00	27.85
ATOM	641	2SG	CME	279	11.574	8.053	17.229	1.00	28.77
ATOM	642	2CB	CME	279	9.954	7.230	17.445	1.00	24.45
ATOM	643	2CA	CME	279	9.943	5.999	18.329	1.00	22.60
ATOM	644	OG	CME	279	10.230	6.331	19.673	1.00	21.99
ATOM	645	N	SER	280	15.075	3.788	18.256	1.00	32.02
ATOM	646	CA	SER	280	15.171	2.566	19.054	1.00	31.88
ATOM	647	CB	SER	280	16.161	1.604	18.408	1.00	32.23
ATOM	648	OG	SER	280	17.471	2.145	18.447	1.00	33.11
ATOM	649	C	SER	280	15.637	2.873	20.467	1.00	32.76
ATOM	650	O	SER	280	15.710	1.978	21.299	1.00	34.40
ATOM	651	N	GLY	281	16.014	4.127	20.710	1.00	33.60
ATOM	652	CA	GLY	281	16.479	4.540	22.022	1.00	33.70
ATOM	653	C	GLY	281	15.357	4.781	23.017	1.00	34.64
ATOM	654	O	GLY	281	15.609	4.974	24.210	1.00	35.32
ATOM	655	N	GLY	282	14.119	4.767	22.531	1.00	34.83
ATOM	656	CA	GLY	282	12.963	4.979	23.388	1.00	34.77
ATOM	657	C	GLY	282	11.697	4.820	22.571	1.00	34.68
ATOM	658	O	GLY	282	11.780	4.727	21.346	1.00	36.05
ATOM	659	N	ALA	283	10.536	4.761	23.222	1.00	33.24
ATOM	660	CA	ALA	283	9.276	4.615	22.495	1.00	32.26
ATOM	661	CB	ALA	283	8.515	3.397	22.983	1.00	34.72
ATOM	662	C	ALA	283	8.479	5.879	22.732	1.00	31.42
ATOM	663	O	ALA	283	8.072	6.157	23.857	1.00	33.31
ATOM	664	N	TYR	284	8.286	6.655	21.673	1.00	29.86
ATOM	665	CA	TYR	284	7.590	7.930	21.756	1.00	26.87
ATOM	666	CB	TYR	284	8.586	9.068	21.499	1.00	25.67
ATOM	667	CG	TYR	284	9.898	8.953	22.270	1.00	25.12
ATOM	668	CD1	TYR	284	11.066	8.484	21.650	1.00	24.08
ATOM	669	CE1	TYR	284	12.280	8.406	22.342	1.00	23.42
ATOM	670	CD2	TYR	284	9.977	9.338	23.611	1.00	25.92
ATOM	671	CE2	TYR	284	11.186	9.263	24.316	1.00	26.34
ATOM	672	CZ	TYR	284	12.334	8.800	23.675	1.00	27.01
ATOM	673	OH	TYR	284	13.526	8.765	24.383	1.00	26.66
ATOM	674	C	TYR	284	6.501	7.977	20.706	1.00	27.07
ATOM	675	O	TYR	284	6.697	7.507	19.583	1.00	27.54
ATOM	676	N	ASP	285	5.360	8.562	21.060	1.00	26.33
ATOM	677	CA	ASP	285	4.237	8.665	20.128	1.00	25.48
ATOM	678	CB	ASP	285	2.906	8.695	20.888	1.00	27.66
ATOM	679	CG	ASP	285	2.754	7.540	21.867	1.00	29.66
ATOM	680	OD1	ASP	285	2.833	6.357	21.451	1.00	30.75
ATOM	681	OD2	ASP	285	2.537	7.822	23.060	1.00	30.49
ATOM	682	C	ASP	285	4.365	9.942	19.308	1.00	24.75
ATOM	683	O	ASP	285	4.021	9.982	18.122	1.00	24.16
ATOM	684	N	ILE	286	4.864	10.991	19.957	1.00	24.04
ATOM	685	CA	ILE	286	5.025	12.289	19.321	1.00	22.60
ATOM	686	CB	ILE	286	4.036	13.310	19.936	1.00	21.83
ATOM	687	CG2	ILE	286	4.185	14.677	19.265	1.00	19.78
ATOM	688	CG1	ILE	286	2.601	12.776	19.805	1.00	20.82
ATOM	689	CD1	ILE	286	1.539	13.664	20.395	1.00	19.00
ATOM	690	C	ILE	286	6.459	12.804	19.470	1.00	22.69
ATOM	691	O	ILE	286	7.052	12.730	20.556	1.00	22.52

ATOM	692	N	ILE	287	7.028	13.274	18.361	1.00	22.96
ATOM	693	CA	ILE	287	8.381	13.822	18.373	1.00	22.01
ATOM	694	CB	ILE	287	9.375	13.029	17.459	1.00	21.82
ATOM	695	CG2	ILE	287	10.741	13.732	17.432	1.00	20.37
ATOM	696	CG1	ILE	287	9.543	11.586	17.945	1.00	20.76
ATOM	697	CD1	ILE	287	8.661	10.601	17.227	1.00	19.72
ATOM	698	C	ILE	287	8.348	15.267	17.890	1.00	20.35
ATOM	699	O	ILE	287	7.944	15.540	16.756	1.00	18.88
ATOM	700	N	ILE	288	8.746	16.184	18.763	1.00	20.27
ATOM	701	CA	ILE	288	8.792	17.595	18.420	1.00	22.23
ATOM	702	CB	ILE	288	8.399	18.525	19.624	1.00	24.13
ATOM	703	CG2	ILE	288	8.370	19.992	19.183	1.00	23.03
ATOM	704	CG1	ILE	288	7.041	18.132	20.224	1.00	25.74
ATOM	705	CD1	ILE	288	5.866	18.329	19.292	1.00	27.52
ATOM	706	C	ILE	288	10.247	17.883	18.076	1.00	20.12
ATOM	707	O	ILE	288	11.118	17.740	18.925	1.00	20.16
ATOM	708	N	CYS	289	10.514	18.173	16.810	1.00	20.26
ATOM	709	CA	CYS	289	11.855	18.520	16.349	1.00	19.98
ATOM	710	CB	CYS	289	12.057	18.095	14.899	1.00	18.98
ATOM	711	SG	CYS	289	12.188	16.314	14.684	1.00	18.93
ATOM	712	C	CYS	289	11.916	20.030	16.466	1.00	20.28
ATOM	713	O	CYS	289	11.550	20.757	15.542	1.00	21.53
ATOM	714	N	ASP	290	12.322	20.482	17.642	1.00	20.55
ATOM	715	CA	ASP	290	12.407	21.892	17.969	1.00	22.05
ATOM	716	CB	ASP	290	12.530	22.030	19.490	1.00	22.57
ATOM	717	CG	ASP	290	12.197	23.413	19.979	1.00	24.81
ATOM	718	OD1	ASP	290	12.731	23.789	21.040	1.00	25.61
ATOM	719	OD2	ASP	290	11.410	24.127	19.312	1.00	27.06
ATOM	720	C	ASP	290	13.564	22.591	17.247	1.00	22.93
ATOM	721	O	ASP	290	14.611	21.983	17.004	1.00	24.56
ATOM	722	N	GLU	291	13.364	23.866	16.905	1.00	22.47
ATOM	723	CA	GLU	291	14.361	24.674	16.190	1.00	21.59
ATOM	724	CB	GLU	291	15.600	24.947	17.055	1.00	22.46
ATOM	725	CG	GLU	291	15.341	25.261	18.533	1.00	23.21
ATOM	726	CD	GLU	291	14.639	26.573	18.786	1.00	24.42
ATOM	727	OE1	GLU	291	14.159	27.222	17.840	1.00	27.28
ATOM	728	OE2	GLU	291	14.552	26.961	19.964	1.00	28.33
ATOM	729	C	GLU	291	14.783	23.938	14.922	1.00	20.30
ATOM	730	O	GLU	291	15.945	23.954	14.535	1.00	20.16
ATOM	731	N	CYS	292	13.804	23.375	14.228	1.00	20.51
ATOM	732	CA	CYS	292	14.057	22.608	13.021	1.00	20.48
ATOM	733	CB	CYS	292	12.762	21.929	12.573	1.00	21.07
ATOM	734	SG	CYS	292	11.485	23.089	12.067	1.00	22.23
ATOM	735	C	CYS	292	14.682	23.411	11.880	1.00	19.98
ATOM	736	O	CYS	292	14.876	22.906	10.777	1.00	18.04
ATOM	737	N	HIS	293	14.962	24.683	12.144	1.00	22.14
ATOM	738	CA	HIS	293	15.592	25.557	11.157	1.00	22.17
ATOM	739	CB	HIS	293	15.198	27.009	11.419	1.00	20.03
ATOM	740	CG	HIS	293	15.713	27.534	12.718	1.00	20.67
ATOM	741	CD2	HIS	293	16.944	27.991	13.068	1.00	20.00
ATOM	742	ND1	HIS	293	14.962	27.549	13.368	1.00	21.26
ATOM	743	CE1	HIS	293	15.701	27.986	14.372	1.00	21.37
ATOM	744	NE2	HIS	293	16.907	28.261	14.413	1.00	20.16
ATOM	745	C	HIS	293	17.121	25.434	11.259	1.00	22.50
ATOM	746	O	HIS	293	17.834	25.959	10.414	1.00	23.46
ATOM	747	N	SER	294	17.611	24.787	12.319	1.00	23.32
ATOM	748	CA	SER	294	19.049	24.621	12.553	1.00	23.42
ATOM	749	CB	SER	294	19.294	23.913	13.878	1.00	21.98

ATOM	750	OG	SER	294	18.708	24.650	14.930	1.00	25.79
ATOM	751	C	SER	294	19.767	23.878	11.441	1.00	24.00
ATOM	752	O	SER	294	19.379	22.774	11.061	1.00	24.59
ATOM	753	N	THR	295	20.845	24.473	10.946	1.00	24.29
ATOM	754	CA	THR	295	21.590	23.866	9.868	1.00	24.56
ATOM	755	CB	THR	295	21.764	24.855	8.697	1.00	25.03
ATOM	756	OG1	THR	295	22.307	26.091	9.175	1.00	24.69
ATOM	757	CG2	THR	295	20.411	25.132	8.038	1.00	24.54
ATOM	758	C	THR	295	22.916	23.247	10.297	1.00	25.11
ATOM	759	O	THR	295	23.773	22.952	9.467	1.00	25.90
ATOM	760	N	ASP	296	23.083	23.035	11.596	1.00	24.58
ATOM	761	CA	ASP	296	24.297	22.405	12.097	1.00	25.65
ATOM	762	CB	ASP	296	24.430	22.642	13.593	1.00	28.87
ATOM	763	CG	ASP	296	23.307	22.010	14.372	1.00	32.27
ATOM	764	OD1	ASP	296	22.182	22.547	14.308	1.00	34.23
ATOM	765	OD2	ASP	296	23.541	20.956	15.009	1.00	35.53
ATOM	766	C	ASP	296	24.142	20.904	11.806	1.00	24.87
ATOM	767	O	ASP	296	23.027	20.374	11.883	1.00	24.43
ATOM	768	N	ALA	297	25.251	20.220	11.524	1.00	23.24
ATOM	769	CA	ALA	297	25.228	18.796	11.185	1.00	22.47
ATOM	770	CB	ALA	297	26.633	18.247	11.066	1.00	20.82
ATOM	771	C	ALA	297	24.414	17.923	12.122	1.00	21.78
ATOM	772	O	ALA	297	23.643	17.079	11.672	1.00	22.68
ATOM	773	N	THR	298	24.571	18.134	13.420	1.00	22.79
ATOM	774	CA	THR	298	23.846	17.338	14.404	1.00	24.28
ATOM	775	CB	THR	298	24.334	17.649	15.813	1.00	24.90
ATOM	776	OG1	THR	298	25.767	17.588	15.822	1.00	26.90
ATOM	777	CG2	THR	298	23.780	16.639	16.800	1.00	24.31
ATOM	778	C	THR	298	22.320	17.460	14.321	1.00	21.89
ATOM	779	O	THR	298	21.614	16.458	14.441	1.00	21.95
ATOM	780	N	SER	299	21.817	18.665	14.074	1.00	20.47
ATOM	781	CA	SER	299	20.373	18.865	13.969	1.00	19.52
ATOM	782	CB	SER	299	20.025	20.352	14.038	1.00	16.97
ATOM	783	OG	SER	299	20.393	20.874	15.300	1.00	15.99
ATOM	784	C	SER	299	19.835	18.243	12.688	1.00	18.61
ATOM	785	C	SER	299	18.810	17.570	12.698	1.00	18.83
ATOM	786	N	ILE	300	20.567	18.418	11.597	1.00	18.65
ATOM	787	CA	ILE	300	20.155	17.863	10.322	1.00	19.88
ATOM	788	CB	ILE	300	21.085	18.343	9.190	1.00	20.48
ATOM	789	CG2	ILE	300	20.691	17.693	7.846	1.00	19.34
ATOM	790	CG1	ILE	300	21.022	19.867	9.098	1.00	19.44
ATOM	791	CD1	ILE	300	22.063	20.436	8.226	1.00	20.43
ATOM	792	C	ILE	300	20.135	16.337	10.358	1.00	20.31
ATOM	793	O	ILE	300	19.194	15.717	9.867	1.00	21.85
ATOM	794	N	LEU	301	21.161	15.733	10.950	1.00	20.00
ATOM	795	CA	LEU	301	21.243	14.280	11.022	1.00	19.61
ATOM	796	CB	LEU	301	22.626	13.852	11.516	1.00	20.91
ATOM	797	CG	LEU	301	22.986	12.379	11.326	1.00	23.01
ATOM	798	CD1	LEU	301	23.023	12.031	9.851	1.00	21.44
ATOM	799	CD2	LEU	301	24.336	12.111	11.964	1.00	24.76
ATOM	800	C	LEU	301	20.156	13.742	11.942	1.00	19.65
ATOM	801	O	LEU	301	19.517	12.729	11.642	1.00	19.47
ATOM	802	N	GLY	302	19.929	14.450	13.044	1.00	19.18
ATOM	803	CA	GLY	302	18.919	14.048	14.002	1.00	18.63
ATOM	804	C	GLY	302	17.522	14.119	13.425	1.00	19.58
ATOM	805	O	GLY	302	16.731	13.194	13.606	1.00	20.16
ATOM	806	N	ILE	303	17.220	15.205	12.719	1.00	19.27
ATOM	807	CA	ILE	303	15.906	15.383	12.113	1.00	19.24

ATOM	808	CB	ILE	303	15.732	16.799	11.518	1.00	18.46
ATOM	809	CG2	ILE	303	14.466	16.879	10.680	1.00	19.48
ATOM	810	CG1	ILE	303	15.646	17.818	12.653	1.00	18.58
ATOM	811	CD1	ILE	303	15.483	19.232	12.199	1.00	19.42
ATOM	812	C	ILE	303	15.675	14.324	11.057	1.00	19.21
ATOM	813	O	ILE	303	14.631	13.685	11.044	1.00	21.27
ATOM	814	N	GLY	304	16.662	14.120	10.191	1.00	20.04
ATOM	815	CA	GLY	304	16.547	13.110	9.160	1.00	20.49
ATOM	816	C	GLY	304	16.323	11.730	9.765	1.00	21.95
ATOM	817	O	GLY	304	15.555	10.930	9.226	1.00	22.92
ATOM	818	N	THR	305	17.009	11.435	10.869	1.00	22.89
ATOM	819	CA	THR	305	16.854	10.150	11.552	1.00	23.21
ATOM	820	CB	THR	305	17.722	10.087	12.830	1.00	22.58
ATOM	821	OG1	THR	305	19.101	10.155	12.458	1.00	26.30
ATOM	822	CG2	THR	305	17.494	8.794	13.603	1.00	20.55
ATOM	823	C	THR	305	15.377	9.988	11.919	1.00	23.59
ATOM	824	O	THR	305	14.734	9.028	11.504	1.00	22.98
ATOM	825	N	VAL	306	14.830	10.974	12.632	1.00	24.39
ATOM	826	CA	VAL	306	13.423	10.954	13.039	1.00	22.55
ATOM	827	CB	VAL	306	13.022	12.258	13.751	1.00	19.96
ATOM	828	CG1	VAL	306	11.516	12.293	13.977	1.00	19.45
ATOM	829	CG2	VAL	306	13.748	12.380	15.061	1.00	18.75
ATOM	830	C	VAL	306	12.499	10.773	11.837	1.00	21.61
ATOM	831	O	VAL	306	11.629	9.908	11.840	1.00	22.37
ATOM	832	N	LEU	307	12.701	11.581	10.805	1.00	21.43
ATOM	833	CA	LEU	307	11.855	11.513	9.622	1.00	21.34
ATOM	834	CB	LEU	307	12.238	12.605	8.626	1.00	19.20
ATOM	835	CG	LEU	307	11.804	14.002	9.057	1.00	17.60
ATOM	836	CD1	LEU	307	12.361	15.033	8.111	1.00	17.57
ATOM	837	CD2	LEU	307	10.293	14.074	9.095	1.00	16.93
ATOM	838	C	LEU	307	11.891	10.155	8.960	1.00	22.33
ATOM	839	O	LEU	307	10.875	9.661	8.490	1.00	24.71
ATOM	840	N	ASP	308	13.051	9.522	8.971	1.00	23.84
ATOM	841	CA	ASP	308	13.184	8.221	8.356	1.00	23.32
ATOM	842	CB	ASP	308	14.655	7.938	8.062	1.00	23.50
ATOM	843	CG	ASP	308	14.859	6.634	7.316	1.00	23.73
ATOM	844	OD1	ASP	308	14.468	6.559	6.136	1.00	25.35
ATOM	845	OD2	ASP	308	15.403	5.682	7.907	1.00	22.72
ATOM	846	C	ASP	308	12.617	7.111	9.230	1.00	23.73
ATOM	847	O	ASP	308	11.878	6.259	8.752	1.00	24.61
ATOM	848	N	GLN	309	12.927	7.159	10.518	1.00	23.54
ATOM	849	CA	GLN	309	12.529	6.130	11.465	1.00	24.40
ATOM	850	CB	GLN	309	13.609	6.003	12.538	1.00	24.46
ATOM	851	CG	GLN	309	14.985	5.638	12.022	1.00	24.18
ATOM	852	CD	GLN	309	16.023	5.622	13.128	1.00	23.84
ATOM	853	OE1	GLN	309	15.702	5.805	14.301	1.00	24.42
ATOM	854	NE2	GLN	309	17.276	5.415	12.760	1.00	25.37
ATOM	855	C	GLN	309	11.169	6.173	12.168	1.00	26.09
ATOM	856	O	GLN	309	10.530	5.116	12.401	1.00	25.68
ATOM	857	N	ALA	310	10.698	7.367	12.537	1.00	27.06
ATOM	858	CA	ALA	310	9.432	7.554	13.273	1.00	23.07
ATOM	859	CB	ALA	310	8.983	9.012	13.224	1.00	27.02
ATOM	860	C	ALA	310	8.251	6.646	12.956	1.00	28.11
ATOM	861	O	ALA	310	7.831	5.866	13.314	1.00	28.35
ATOM	862	N	GLU	311	7.714	6.735	11.742	1.00	29.49
ATOM	863	CA	GLU	311	6.560	5.916	11.376	1.00	31.72
ATOM	864	CB	GLU	311	6.125	6.161	9.932	1.00	31.31
ATOM	865	CG	GLU	311	4.847	5.405	9.558	1.00	33.59

ATOM	866	CD	GLU	311	4.180	5.925	8.291	1.00	34.98
ATOM	867	OE1	GLU	311	2.993	5.602	8.065	1.00	36.53
ATOM	868	OE2	GLU	311	4.834	6.657	7.519	1.00	37.12
ATOM	869	C	GLU	311	6.784	4.429	11.614	1.00	33.13
ATOM	870	O	GLU	311	5.993	3.784	12.303	1.00	35.45
ATOM	871	N	THR	312	7.880	3.898	11.085	1.00	32.86
ATOM	872	CA	THR	312	8.200	2.487	11.249	1.00	32.32
ATOM	873	CB	THR	312	9.488	2.140	10.477	1.00	32.72
ATOM	874	OG1	THR	312	9.289	2.449	9.092	1.00	33.20
ATOM	875	CG2	THR	312	9.829	0.661	10.611	1.00	31.35
ATOM	876	C	THR	312	8.329	2.104	12.727	1.00	31.60
ATOM	877	O	THR	312	8.016	0.980	13.114	1.00	32.69
ATOM	878	N	ALA	313	8.741	3.057	13.554	1.00	30.31
ATOM	879	CA	ALA	313	8.899	2.806	14.977	1.00	29.28
ATOM	880	CB	ALA	313	9.949	3.731	15.563	1.00	28.71
ATOM	881	C	ALA	313	7.575	2.950	15.722	1.00	28.65
ATOM	882	O	ALA	313	7.520	2.786	16.939	1.00	29.03
ATOM	883	N	GLY	314	6.514	3.278	14.996	1.00	28.36
ATOM	884	CA	GLY	314	5.207	3.409	15.618	1.00	29.07
ATOM	885	C	GLY	314	4.836	4.749	16.231	1.00	28.95
ATOM	886	O	GLY	314	4.048	4.822	17.173	1.00	28.57
ATOM	887	N	ALA	315	5.418	5.821	15.724	1.00	29.15
ATOM	888	CA	ALA	315	5.080	7.131	16.239	1.00	27.89
ATOM	889	CB	ALA	315	6.218	8.106	15.987	1.00	27.99
ATOM	890	C	ALA	315	3.820	7.561	15.499	1.00	27.19
ATOM	891	O	ALA	315	3.509	7.042	14.421	1.00	25.84
ATOM	892	N	ARG	316	3.090	8.493	16.092	1.00	27.55
ATOM	893	CA	ARG	316	1.863	9.010	15.502	1.00	27.08
ATOM	894	CB	ARG	316	0.777	9.155	16.582	1.00	31.00
ATOM	895	CG	ARG	316	-0.529	9.805	16.099	1.00	35.35
ATOM	896	CD	ARG	316	-1.404	8.835	15.306	1.00	38.97
ATOM	897	NE	ARG	316	-1.989	7.798	16.158	1.00	42.10
ATOM	898	CZ	ARG	316	-2.953	8.008	17.055	1.00	43.29
ATOM	899	NH1	ARG	316	-3.462	9.220	17.232	1.00	43.63
ATOM	900	NH2	ARG	316	-3.393	7.004	17.799	1.00	43.76
ATOM	901	C	ARG	316	2.095	10.366	14.854	1.00	25.15
ATOM	902	O	ARG	316	1.521	10.679	13.805	1.00	25.12
ATOM	903	N	LEU	317	2.962	11.164	15.457	1.00	22.37
ATOM	904	CA	LEU	317	3.185	12.493	14.931	1.00	20.99
ATOM	905	CB	LEU	317	2.234	13.482	15.648	1.00	18.70
ATOM	906	CG	LEU	317	2.297	14.999	15.402	1.00	16.65
ATOM	907	CD1	LEU	317	1.898	15.327	13.972	1.00	15.36
ATOM	908	CD2	LEU	317	1.384	15.723	16.375	1.00	16.28
ATOM	909	C	LEU	317	4.612	12.987	15.060	1.00	21.09
ATOM	910	O	LEU	317	5.293	12.705	16.053	1.00	21.51
ATOM	911	N	VAL	318	5.061	13.686	14.020	1.00	20.92
ATOM	912	CA	VAL	318	6.368	14.319	14.009	1.00	21.69
ATOM	913	CB	VAL	318	7.324	13.760	12.924	1.00	21.79
ATOM	914	CG1	VAL	318	8.541	14.686	12.772	1.00	20.61
ATOM	915	CG2	VAL	318	7.801	12.375	13.320	1.00	21.19
ATOM	916	C	VAL	318	6.061	15.737	13.736	1.00	21.64
ATOM	917	O	VAL	318	5.367	16.112	12.767	1.00	20.75
ATOM	918	N	VAL	319	6.523	16.660	14.626	1.00	21.64
ATOM	919	CA	VAL	319	6.291	18.088	14.489	1.00	21.71
ATOM	920	CB	VAL	319	5.581	18.679	15.751	1.00	21.72
ATOM	921	CG1	VAL	319	5.321	20.171	15.579	1.00	19.36
ATOM	922	CG2	VAL	319	4.280	17.947	16.020	1.00	21.02
ATOM	923	C	VAL	319	7.619	18.793	14.308	1.00	20.25

ATOM	924	O	VAL	319	8.520	18.635	15.127	1.00	19.92
ATOM	925	N	LEU	320	7.739	19.555	13.226	1.00	20.09
ATOM	926	CA	LEU	320	8.946	20.323	12.934	1.00	18.99
ATOM	927	CB	LEU	320	9.276	20.236	11.442	1.00	18.78
ATOM	928	CG	LEU	320	9.265	18.835	10.803	1.00	20.01
ATOM	929	CD1	LEU	320	9.449	18.951	9.309	1.00	20.04
ATOM	930	CD2	LEU	320	10.342	17.940	11.400	1.00	20.17
ATOM	931	C	LEU	320	8.609	21.754	13.352	1.00	17.86
ATOM	932	O	LEU	320	7.887	22.459	12.655	1.00	17.59
ATOM	933	N	ALA	321	9.102	22.160	14.515	1.00	18.47
ATOM	934	CA	ALA	321	8.807	23.476	15.055	1.00	20.27
ATOM	935	CB	ALA	321	8.365	23.354	16.522	1.00	19.53
ATOM	936	C	ALA	321	9.926	24.499	14.935	1.00	22.46
ATOM	937	O	ALA	321	11.105	24.199	15.192	1.00	22.78
ATOM	938	N	THR	322	9.531	25.732	14.615	1.00	23.57
ATOM	939	CA	THR	322	10.463	26.839	14.463	1.00	24.42
ATOM	940	CB	THR	322	11.384	26.632	13.224	1.00	23.87
ATOM	941	OG1	THR	322	12.368	27.677	13.159	1.00	22.26
ATOM	942	CG2	THR	322	10.561	26.606	11.935	1.00	20.90
ATOM	943	C	THR	322	9.721	28.166	14.301	1.00	25.40
ATOM	944	O	THR	322	8.632	28.227	13.719	1.00	25.14
ATOM	945	N	ALA	323	10.317	29.220	14.841	1.00	25.81
ATOM	946	CA	ALA	323	9.768	30.559	14.729	1.00	25.79
ATOM	947	CB	ALA	323	10.219	31.412	15.902	1.00	25.93
ATOM	948	C	ALA	323	10.288	31.153	13.423	1.00	26.98
ATOM	949	O	ALA	323	9.758	32.153	12.932	1.00	28.83
ATOM	950	N	THR	324	11.325	30.531	12.862	1.00	25.90
ATOM	951	CA	THR	324	11.925	31.003	11.617	1.00	24.88
ATOM	952	CB	THR	324	13.319	31.611	11.876	1.00	24.01
ATOM	953	OG1	THR	324	14.106	30.689	12.641	1.00	25.50
ATOM	954	CG2	THR	324	13.201	32.908	12.648	1.00	23.67
ATOM	955	C	THR	324	12.048	29.943	10.508	1.00	24.40
ATOM	956	O	THR	324	13.123	29.369	10.293	1.00	24.97
ATOM	957	N	PRO	325	10.935	29.624	9.829	1.00	22.47
ATOM	958	CD	PRO	325	9.557	30.088	10.041	1.00	21.14
ATOM	959	CA	PRO	325	10.978	28.634	8.755	1.00	22.40
ATOM	960	CB	PRO	325	9.500	28.446	8.422	1.00	20.85
ATOM	961	CG	PRO	325	8.922	29.769	8.720	1.00	19.94
ATOM	962	C	PRO	325	11.756	29.190	7.559	1.00	23.10
ATOM	963	O	PRO	325	12.008	30.396	7.486	1.00	23.30
ATOM	964	N	PRO	326	12.159	28.319	6.609	1.00	23.99
ATOM	965	CD	PRO	326	12.034	26.849	6.583	1.00	23.51
ATOM	966	CA	PRO	326	12.908	28.793	5.437	1.00	23.61
ATOM	967	CB	PRO	326	12.949	27.553	4.544	1.00	22.60
ATOM	968	CG	PRO	326	13.058	26.456	5.545	1.00	22.79
ATOM	969	C	PRO	326	12.245	29.985	4.740	1.00	22.55
ATOM	970	O	PRO	326	11.019	30.087	4.696	1.00	23.41
ATOM	971	N	GLY	327	13.070	30.901	4.249	1.00	20.16
ATOM	972	CA	GLY	327	12.576	32.077	3.561	1.00	20.04
ATOM	973	C	GLY	327	12.224	33.207	4.501	1.00	20.56
ATOM	974	O	GLY	327	11.681	34.216	4.075	1.00	21.64
ATOM	975	N	SER	328	12.544	33.044	5.779	1.00	22.07
ATOM	976	CA	SER	328	12.245	34.056	6.783	1.00	21.35
ATOM	977	CB	SER	328	12.379	33.466	8.139	1.00	20.72
ATOM	978	OG	SER	328	11.326	32.565	8.454	1.00	20.21
ATOM	979	C	SER	328	13.088	35.322	6.689	1.00	22.21
ATOM	980	O	SER	328	14.185	35.333	6.115	1.00	21.32
ATOM	981	N	VAL	329	12.552	36.337	7.275	1.00	21.78

ATOM	982	CA	VAL	329	13.207	37.678	7.325	1.00	21.67
ATOM	983	CB	VAL	329	12.634	38.651	6.278	1.00	21.56
ATOM	984	CG1	VAL	329	13.039	38.203	4.867	1.00	21.42
ATOM	985	CG2	VAL	329	11.123	38.747	6.410	1.00	19.14
ATOM	986	C	VAL	329	12.960	38.192	8.737	1.00	21.96
ATOM	987	O	VAL	329	12.080	37.683	9.424	1.00	21.78
ATOM	988	N	THR	330	13.786	39.132	9.187	1.00	23.09
ATOM	989	CA	THR	330	13.681	39.708	10.523	1.00	24.47
ATOM	990	CB	THR	330	15.073	40.131	11.047	1.00	24.34
ATOM	991	OG1	THR	330	15.958	39.009	10.972	1.00	25.56
ATOM	992	CG2	THR	330	14.997	40.577	12.490	1.00	23.96
ATOM	993	C	THR	330	12.719	40.888	10.521	1.00	25.81
ATOM	994	O	THR	330	13.062	42.014	10.134	1.00	25.19
ATOM	995	N	VAL	331	11.507	40.600	10.972	1.00	27.46
ATOM	996	CA	VAL	331	10.415	41.558	11.029	1.00	29.93
ATOM	997	CB	VAL	331	9.065	40.789	10.871	1.00	30.69
ATOM	998	CG1	VAL	331	7.885	41.620	11.359	1.00	33.40
ATOM	999	CG2	VAL	331	8.871	40.366	9.408	1.00	28.41
ATOM	1000	C	VAL	331	10.431	42.356	12.330	1.00	30.66
ATOM	1001	O	VAL	331	10.942	41.880	13.347	1.00	30.44
ATOM	1002	N	PRO	332	9.923	43.601	12.296	1.00	31.80
ATOM	1003	CD	PRO	332	9.525	44.351	11.088	1.00	32.94
ATOM	1004	CA	PRO	332	9.868	44.471	13.469	1.00	32.90
ATOM	1005	CB	PRO	332	8.882	45.544	13.029	1.00	33.03
ATOM	1006	CG	PRO	332	9.299	45.772	11.616	1.00	32.19
ATOM	1007	C	PRO	332	9.403	43.751	14.726	1.00	33.35
ATOM	1008	O	PRO	332	8.539	42.879	14.673	1.00	33.22
ATOM	1009	N	HIS	333	10.042	44.092	15.840	1.00	34.93
ATOM	1010	CA	HIS	333	9.747	43.526	17.149	1.00	35.66
ATOM	1011	CB	HIS	333	11.040	43.034	17.801	1.00	35.75
ATOM	1012	CG	HIS	333	10.864	42.519	19.196	1.00	35.91
ATOM	1013	CD2	HIS	333	11.036	41.281	19.717	1.00	37.50
ATOM	1014	ND1	HIS	333	10.494	43.327	20.250	1.00	35.51
ATOM	1015	CE1	HIS	333	10.448	42.610	21.359	1.00	35.57
ATOM	1016	NE2	HIS	333	10.774	41.366	21.063	1.00	37.41
ATOM	1017	C	HIS	333	9.152	44.666	17.967	1.00	36.79
ATOM	1018	O	HIS	333	9.616	45.804	17.878	1.00	37.38
ATOM	1019	N	PRO	334	8.174	44.362	18.833	1.00	37.08
ATOM	1020	CD	PRO	334	7.664	43.006	19.111	1.00	36.74
ATOM	1021	CA	PRO	334	7.509	45.364	19.680	1.00	37.36
ATOM	1022	CB	PRO	334	6.622	44.508	20.589	1.00	38.15
ATOM	1023	CG	PRO	334	6.344	43.286	19.753	1.00	38.80
ATOM	1024	C	PRO	334	8.458	46.225	20.521	1.00	37.12
ATOM	1025	O	PRO	334	8.426	47.448	20.447	1.00	37.73
ATOM	1026	N	ASN	335	9.283	45.564	21.330	1.00	36.19
ATOM	1027	CA	ASN	335	10.231	46.226	22.228	1.00	35.31
ATOM	1028	CB	ASN	335	10.616	45.294	23.385	1.00	36.70
ATOM	1029	CG	ASN	335	9.433	44.782	24.146	1.00	38.17
ATOM	1030	OD1	ASN	335	8.393	45.429	24.192	1.00	41.02
ATOM	1031	ND2	ASN	335	9.579	43.602	24.751	1.00	37.75
ATOM	1032	C	ASN	335	11.547	46.676	21.640	1.00	33.43
ATOM	1033	O	ASN	335	12.410	47.100	22.404	1.00	35.07
ATOM	1034	N	ILE	336	11.732	46.613	20.325	1.00	30.99
ATOM	1035	CA	ILE	336	13.043	46.972	19.733	1.00	27.79
ATOM	1036	CB	ILE	336	13.771	45.706	19.242	1.00	26.56
ATOM	1037	CG2	ILE	336	15.209	46.038	18.647	1.00	23.81
ATOM	1038	CG1	ILE	336	13.786	44.609	20.312	1.00	24.10
ATOM	1039	CD1	ILE	336	14.260	43.272	19.819	1.00	22.21

ATOM	1040	C	ILE	336	13.131	48.077	18.738	1.00	28.12
ATOM	1041	O	ILE	336	12.731	47.896	17.588	1.00	28.53
ATOM	1042	N	GLU	337	13.694	49.213	19.128	1.00	27.62
ATOM	1043	CA	GLU	337	13.879	50.309	18.189	1.00	28.28
ATOM	1044	CB	GLU	337	14.019	51.634	18.931	1.00	29.84
ATOM	1045	CG	GLU	337	14.335	52.802	18.002	1.00	33.89
ATOM	1046	CD	GLU	337	14.754	54.067	18.730	1.00	36.64
ATOM	1047	OE1	GLU	337	14.866	54.049	19.978	1.00	39.22
ATOM	1048	OE2	GLU	337	14.987	55.084	18.041	1.00	38.86
ATOM	1049	C	GLU	337	15.168	50.031	17.401	1.00	27.48
ATOM	1050	O	GLU	337	16.224	49.807	17.990	1.00	27.75
ATOM	1051	N	GLU	338	15.092	50.053	16.078	1.00	26.13
ATOM	1052	CA	GLU	338	16.264	49.791	15.260	1.00	25.01
ATOM	1053	CB	GLU	338	15.939	48.745	14.200	1.00	25.16
ATOM	1054	CG	GLU	338	15.433	47.431	14.770	1.00	26.26
ATOM	1055	CD	GLU	338	15.271	46.355	13.720	1.00	25.40
ATOM	1056	OE1	GLU	338	14.396	45.490	13.896	1.00	26.96
ATOM	1057	OE2	GLU	338	16.020	46.363	12.723	1.00	26.71
ATOM	1058	C	GLU	338	16.794	51.050	14.594	1.00	25.30
ATOM	1059	O	GLU	338	16.033	51.835	14.033	1.00	27.51
ATOM	1060	N	VAL	339	18.103	51.250	14.646	1.00	24.09
ATOM	1061	CA	VAL	339	18.690	52.421	14.027	1.00	22.82
ATOM	1062	CB	VAL	339	18.667	53.653	14.986	1.00	22.08
ATOM	1063	CG1	VAL	339	18.756	53.221	16.424	1.00	21.99
ATOM	1064	CG2	VAL	339	19.763	54.646	14.637	1.00	19.75
ATOM	1065	C	VAL	339	20.064	52.174	13.411	1.00	22.67
ATOM	1066	O	VAL	339	20.951	51.593	14.027	1.00	23.55
ATOM	1067	N	ALA	340	20.189	52.567	12.150	1.00	22.35
ATOM	1068	CA	ALA	340	21.416	52.428	11.384	1.00	23.06
ATOM	1069	CB	ALA	340	21.169	52.877	9.952	1.00	20.82
ATOM	1070	C	ALA	340	22.559	53.240	11.969	1.00	23.85
ATOM	1071	O	ALA	340	22.354	54.337	12.485	1.00	25.71
ATOM	1072	N	LEU	341	23.761	52.686	11.929	1.00	23.84
ATOM	1073	CA	LEU	341	24.920	53.417	12.404	1.00	23.48
ATOM	1074	CB	LEU	341	26.069	52.468	12.729	1.00	22.83
ATOM	1075	CG	LEU	341	25.938	51.583	13.960	1.00	21.53
ATOM	1076	CD1	LEU	341	27.012	50.509	13.925	1.00	22.65
ATOM	1077	CD2	LEU	341	26.054	52.427	15.203	1.00	21.05
ATOM	1078	C	LEU	341	25.307	54.276	11.206	1.00	25.07
ATOM	1079	O	LEU	341	24.967	53.939	10.064	1.00	25.58
ATOM	1080	N	SER	342	25.988	55.388	11.459	1.00	25.28
ATOM	1081	CA	SER	342	26.426	56.272	10.391	1.00	25.74
ATOM	1082	CB	SER	342	25.832	57.680	10.569	1.00	25.63
ATOM	1083	OG	SER	342	26.162	58.252	11.831	1.00	26.66
ATOM	1084	C	SER	342	27.946	56.313	10.422	1.00	26.04
ATOM	1085	O	SER	342	28.588	55.459	11.030	1.00	26.02
ATOM	1086	N	THR	343	28.528	57.276	9.727	1.00	27.63
ATOM	1087	CA	THR	343	29.972	57.416	9.712	1.00	28.59
ATOM	1088	CB	THR	343	30.429	58.057	8.404	1.00	29.62
ATOM	1089	OG1	THR	343	29.514	59.101	8.050	1.00	30.43
ATOM	1090	CG2	THR	343	30.455	57.019	7.302	1.00	32.51
ATOM	1091	C	THR	343	30.422	58.275	10.890	1.00	28.11
ATOM	1092	O	THR	343	31.614	58.399	11.171	1.00	29.07
ATOM	1093	N	THR	344	29.459	58.863	11.533	1.00	27.10
ATOM	1094	CA	THR	344	29.767	59.710	12.714	1.00	27.21
ATOM	1095	CB	THR	344	28.729	60.827	12.825	1.00	27.65
ATOM	1096	OG1	THR	344	28.658	61.514	11.568	1.00	28.57
ATOM	1097	CG2	THR	344	29.100	61.805	13.924	1.00	27.24

ATOM	1098	C	THR	344	29.842	58.908	14.008	1.00	27.63
ATOM	1099	O	THR	344	28.884	58.225	14.396	1.00	27.69
ATOM	1100	N	GLY	345	31.003	58.969	14.649	1.00	26.95
ATOM	1101	CA	GLY	345	31.211	58.260	15.890	1.00	26.75
ATOM	1102	C	GLY	345	32.688	58.168	16.189	1.00	28.21
ATOM	1103	O	GLY	345	33.512	58.276	15.285	1.00	28.29
ATOM	1104	N	GLU	346	33.023	57.926	17.451	1.00	28.51
ATOM	1105	CA	GLU	346	34.414	57.832	17.863	1.00	29.04
ATOM	1106	CB	GLU	346	34.541	58.020	19.378	1.00	30.35
ATOM	1107	CG	GLU	346	34.291	59.439	19.880	1.00	32.52
ATOM	1108	CD	GLU	346	32.888	59.926	19.593	1.00	32.87
ATOM	1109	OE1	GLU	346	31.929	59.174	19.854	1.00	32.23
ATOM	1110	OE2	GLU	346	32.747	61.057	19.086	1.00	35.06
ATOM	1111	C	GLU	346	35.084	56.523	17.479	1.00	28.20
ATOM	1112	O	GLU	346	36.283	56.502	17.218	1.00	29.40
ATOM	1113	N	ILE	347	34.321	55.431	17.457	1.00	28.52
ATOM	1114	CA	ILE	347	34.889	54.110	17.153	1.00	26.91
ATOM	1115	CB	ILE	347	34.453	53.035	18.192	1.00	27.90
ATOM	1116	CG2	ILE	347	35.250	51.776	18.005	1.00	28.31
ATOM	1117	CG1	ILE	347	34.645	53.537	19.620	1.00	29.70
ATOM	1118	CD1	ILE	347	33.400	54.194	20.186	1.00	32.81
ATOM	1119	C	ILE	347	34.551	53.550	15.781	1.00	24.52
ATOM	1120	O	ILE	347	33.392	53.258	15.490	1.00	23.00
ATOM	1121	N	PRO	348	35.559	53.398	14.914	1.00	23.86
ATOM	1122	CD	PRO	348	36.947	53.871	15.026	1.00	23.37
ATOM	1123	CA	PRO	348	35.302	52.854	13.582	1.00	24.53
ATOM	1124	CB	PRO	348	36.692	52.834	12.959	1.00	24.34
ATOM	1125	CG	PRO	348	37.338	54.030	13.588	1.00	23.28
ATOM	1126	C	PRO	348	34.759	51.449	13.786	1.00	25.57
ATOM	1127	O	PRO	348	35.290	50.696	14.606	1.00	25.45
ATOM	1128	N	PHE	349	33.677	51.118	13.084	1.00	25.89
ATOM	1129	CA	PHE	349	33.041	49.812	13.216	1.00	24.50
ATOM	1130	CB	PHE	349	31.971	49.860	14.318	1.00	23.29
ATOM	1131	CG	PHE	349	31.358	48.522	14.632	1.00	25.07
ATOM	1132	CD1	PHE	349	32.025	47.610	15.447	1.00	26.07
ATOM	1133	CD2	PHE	349	30.111	48.175	14.119	1.00	25.08
ATOM	1134	CE1	PHE	349	31.461	46.372	15.750	1.00	25.64
ATOM	1135	CE2	PHE	349	29.535	46.945	14.411	1.00	25.25
ATOM	1136	CZ	PHE	349	30.211	46.038	15.230	1.00	26.19
ATOM	1137	C	PHE	349	32.437	49.321	11.904	1.00	23.33
ATOM	1138	O	PHE	349	31.361	49.749	11.501	1.00	22.31
ATOM	1139	N	TYR	350	33.154	48.418	11.247	1.00	23.43
ATOM	1140	CA	TYR	350	32.725	47.820	9.986	1.00	23.78
ATOM	1141	CB	TYR	350	31.636	46.759	10.230	1.00	21.13
ATOM	1142	CG	TYR	350	32.133	45.531	10.967	1.00	20.42
ATOM	1143	CD1	TYR	350	32.302	45.552	12.344	1.00	19.57
ATOM	1144	CE1	TYR	350	32.794	44.440	13.028	1.00	20.40
ATOM	1145	CD2	TYR	350	32.465	44.353	10.279	1.00	21.51
ATOM	1146	CE2	TYR	350	32.963	43.224	10.958	1.00	19.67
ATOM	1147	CZ	TYR	350	33.126	43.282	12.335	1.00	20.56
ATOM	1148	OH	TYR	350	33.648	42.212	13.040	1.00	20.53
ATOM	1149	C	TYR	350	32.280	48.823	8.920	1.00	25.07
ATOM	1150	O	TYR	350	31.215	48.680	8.324	1.00	26.53
ATOM	1151	N	GLY	351	33.118	49.817	8.656	1.00	25.52
ATOM	1152	CA	GLY	351	32.789	50.802	7.644	1.00	26.67
ATOM	1153	C	GLY	351	32.054	52.000	8.205	1.00	27.75
ATOM	1154	O	GLY	351	32.097	53.086	7.624	1.00	29.56
ATOM	1155	N	LYS	352	31.332	51.793	9.300	1.00	28.35

ATOM	1156	CA	LYS	352	30.596	52.858	9.962	1.00	26.46
ATOM	1157	CB	LYS	352	29.182	52.405	10.332	1.00	26.95
ATOM	1158	CG	LYS	352	28.352	51.994	9.145	1.00	28.09
ATOM	1159	CD	LYS	352	28.138	53.145	8.186	1.00	29.10
ATOM	1160	CE	LYS	352	27.767	52.615	6.811	1.00	31.84
ATOM	1161	NZ	LYS	352	26.677	51.594	6.876	1.00	34.67
ATOM	1162	C	LYS	352	31.373	53.197	11.213	1.00	25.16
ATOM	1163	O	LYS	352	32.560	52.903	11.313	1.00	24.74
ATOM	1164	N	ALA	353	30.704	53.811	12.170	1.00	26.04
ATOM	1165	CA	ALA	353	31.353	54.186	13.407	1.00	27.08
ATOM	1166	CB	ALA	353	31.987	55.568	13.267	1.00	26.55
ATOM	1167	C	ALA	353	30.332	54.172	14.533	1.00	27.81
ATOM	1168	O	ALA	353	29.122	54.285	14.297	1.00	29.07
ATOM	1169	N	ILE	354	30.816	53.977	15.750	1.00	26.83
ATOM	1170	CA	ILE	354	29.944	53.949	16.903	1.00	26.78
ATOM	1171	CB	ILE	354	30.136	52.664	17.758	1.00	26.37
ATOM	1172	CG2	ILE	354	29.224	52.705	18.989	1.00	23.34
ATOM	1173	CG1	ILE	354	29.864	51.409	16.922	1.00	26.07
ATOM	1174	CD1	ILE	354	30.151	50.093	17.660	1.00	26.73
ATOM	1175	C	ILE	354	30.269	55.147	17.770	1.00	27.53
ATOM	1176	O	ILE	354	31.446	55.480	17.980	1.00	27.83
ATOM	1177	N	PRO	355	29.231	55.890	18.172	1.00	27.07
ATOM	1178	CD	PRO	355	27.876	55.817	17.601	1.00	26.53
ATOM	1179	CA	PRO	355	29.379	57.069	19.026	1.00	27.16
ATOM	1180	CB	PRO	355	28.042	57.794	18.851	1.00	27.57
ATOM	1181	CG	PRO	355	27.507	57.257	17.531	1.00	28.35
ATOM	1182	C	PRO	355	29.521	56.570	20.463	1.00	27.80
ATOM	1183	O	PRO	355	28.665	55.825	20.951	1.00	28.66
ATOM	1184	N	LEU	356	30.602	56.955	21.133	1.00	27.31
ATOM	1185	CA	LEU	356	30.821	56.537	22.512	1.00	26.78
ATOM	1186	CB	LEU	356	32.024	57.269	23.110	1.00	27.84
ATOM	1187	CG	LEU	356	33.384	56.622	22.838	1.00	27.71
ATOM	1188	CD1	LEU	356	34.515	57.553	23.275	1.00	27.97
ATOM	1189	CD2	LEU	356	33.457	55.297	23.568	1.00	25.40
ATOM	1190	C	LEU	356	29.591	56.787	23.367	1.00	25.92
ATOM	1191	O	LEU	356	29.272	56.004	24.257	1.00	25.15
ATOM	1192	N	ALA	357	28.887	57.872	23.069	1.00	26.25
ATOM	1193	CA	ALA	357	27.685	58.241	23.813	1.00	26.44
ATOM	1194	CB	ALA	357	27.072	59.522	23.228	1.00	25.83
ATOM	1195	C	ALA	357	26.638	57.124	23.873	1.00	26.65
ATOM	1196	O	ALA	357	26.011	56.918	24.911	1.00	26.75
ATOM	1197	N	VAL	358	26.502	56.360	22.791	1.00	26.24
ATOM	1198	CA	VAL	358	25.506	55.295	22.758	1.00	26.40
ATOM	1199	CB	VAL	358	25.119	54.892	21.298	1.00	25.09
ATOM	1200	CG1	VAL	358	24.714	56.119	20.511	1.00	23.26
ATOM	1201	CG2	VAL	358	26.266	54.180	20.597	1.00	24.96
ATOM	1202	C	VAL	358	25.881	54.069	23.590	1.00	26.35
ATOM	1203	O	VAL	358	25.050	53.179	23.797	1.00	27.18
ATOM	1204	N	ILE	359	27.121	54.021	24.074	1.00	25.51
ATOM	1205	CA	ILE	359	27.567	52.892	24.893	1.00	24.89
ATOM	1206	CB	ILE	359	28.582	51.982	24.136	1.00	22.23
ATOM	1207	CG2	ILE	359	27.357	51.199	23.329	1.00	21.17
ATOM	1208	CG1	ILE	359	29.756	52.814	23.600	1.00	21.55
ATOM	1209	CD1	ILE	359	30.892	52.026	22.995	1.00	17.63
ATOM	1210	C	ILE	359	28.159	53.308	26.237	1.00	25.79
ATOM	1211	O	ILE	359	28.437	52.459	27.076	1.00	25.36
ATOM	1212	N	ALA	360	28.304	54.616	26.449	1.00	29.45
ATOM	1213	CA	ALA	360	28.879	55.171	27.681	1.00	31.32

ATOM	1214	CB	ALA	360	28.880	56.691	27.621	1.00	30.01
ATOM	1215	C	ALA	360	28.207	54.684	28.972	1.00	32.84
ATOM	1216	O	ALA	360	28.889	54.369	29.960	1.00	33.70
ATOM	1217	N	GLY	361	26.880	54.659	28.981	1.00	32.93
ATOM	1218	CA	GLY	361	26.172	54.179	30.154	1.00	32.53
ATOM	1219	C	GLY	361	25.285	53.020	29.739	1.00	32.16
ATOM	1220	O	GLY	361	24.892	52.945	28.579	1.00	33.01
ATOM	1221	N	GLY	362	24.978	52.115	30.664	1.00	31.44
ATOM	1222	CA	GLY	362	24.124	50.980	30.352	1.00	28.17
ATOM	1223	C	GLY	362	24.894	49.725	29.979	1.00	28.18
ATOM	1224	O	GLY	362	26.128	49.699	30.060	1.00	28.64
ATOM	1225	N	ARG	363	24.168	48.677	29.597	1.00	25.54
ATOM	1226	CA	ARG	363	24.762	47.404	29.196	1.00	25.19
ATOM	1227	CB	ARG	363	24.135	46.256	29.985	1.00	25.16
ATOM	1228	CG	ARG	363	23.726	46.631	31.401	1.00	26.44
ATOM	1229	CD	ARG	363	23.093	45.460	32.123	1.00	29.20
ATOM	1230	NE	ARG	363	24.075	44.760	32.935	1.00	34.10
ATOM	1231	CZ	ARG	363	24.655	43.608	32.616	1.00	35.13
ATOM	1232	NH1	ARG	363	24.358	42.977	31.494	1.00	34.77
ATOM	1233	NH2	ARG	363	25.613	43.130	33.389	1.00	36.31
ATOM	1234	C	ARG	363	24.504	47.226	27.695	1.00	24.94
ATOM	1235	O	ARG	363	23.377	47.393	27.222	1.00	24.76
ATOM	1236	N	HIS	364	25.542	46.910	26.934	1.00	24.18
ATOM	1237	CA	HIS	364	25.385	46.776	25.494	1.00	23.64
ATOM	1238	CB	HIS	364	25.891	48.048	24.830	1.00	23.19
ATOM	1239	CG	HIS	364	25.367	49.291	25.478	1.00	25.11
ATOM	1240	CD2	HIS	364	25.895	50.084	26.438	1.00	24.33
ATOM	1241	ND1	HIS	364	24.116	49.803	25.205	1.00	26.29
ATOM	1242	CE1	HIS	364	23.894	50.856	25.970	1.00	25.44
ATOM	1243	NE2	HIS	364	24.959	51.047	26.726	1.00	25.09
ATOM	1244	C	HIS	364	26.133	45.559	24.993	1.00	23.60
ATOM	1245	O	HIS	364	27.098	45.128	25.628	1.00	24.11
ATOM	1246	N	LEU	365	25.645	44.976	23.900	1.00	22.16
ATOM	1247	CA	LEU	365	26.247	43.784	23.310	1.00	21.25
ATOM	1248	CB	LEU	365	25.241	42.635	23.316	1.00	20.31
ATOM	1249	CG	LEU	365	25.667	41.278	22.749	1.00	19.06
ATOM	1250	CD1	LEU	365	26.952	40.821	23.413	1.00	18.55
ATOM	1251	CD2	LEU	365	24.562	40.252	22.966	1.00	16.61
ATOM	1252	C	LEU	365	26.672	44.079	21.883	1.00	21.19
ATOM	1253	O	LEU	365	25.836	44.377	21.031	1.00	21.03
ATOM	1254	N	ILE	366	27.966	43.978	21.615	1.00	20.98
ATOM	1255	CA	ILE	366	28.473	44.255	20.283	1.00	21.20
ATOM	1256	CB	ILE	366	29.646	45.254	20.322	1.00	21.57
ATOM	1257	CG2	ILE	366	30.113	45.572	18.911	1.00	19.27
ATOM	1258	CG1	ILE	366	29.225	46.536	21.051	1.00	21.36
ATOM	1259	CD1	ILE	366	30.303	47.607	21.078	1.00	20.61
ATOM	1260	C	ILE	366	28.925	42.974	19.605	1.00	21.06
ATOM	1261	O	ILE	366	29.825	42.296	20.093	1.00	20.15
ATOM	1262	N	PHE	367	28.274	42.635	18.495	1.00	20.98
ATOM	1263	CA	PHE	367	28.610	41.438	17.747	1.00	21.40
ATOM	1264	CB	PHE	367	27.364	40.804	17.125	1.00	20.48
ATOM	1265	CG	PHE	367	26.556	39.975	18.093	1.00	20.75
ATOM	1266	CD1	PHE	367	25.393	40.487	18.671	1.00	20.83
ATOM	1267	CD2	PHE	367	26.951	38.675	18.416	1.00	19.09
ATOM	1268	CE1	PHE	367	24.633	39.711	19.557	1.00	19.99
ATOM	1269	CE2	PHE	367	26.010	37.899	19.291	1.00	19.22
ATOM	1270	CZ	PHE	367	25.043	38.417	19.865	1.00	20.05
ATOM	1271	C	PHE	367	29.644	41.705	16.670	1.00	22.44

ATOM	1272	O	PHE	367	29.478	42.596	15.829	1.00	21.74
ATOM	1273	N	CYS	368	30.728	40.942	16.728	1.00	22.95
ATOM	1274	CA	CYS	368	31.807	41.032	15.761	1.00	23.17
ATOM	1275	CB	CYS	368	33.126	41.385	16.464	1.00	23.99
ATOM	1276	SG	CYS	368	33.120	43.017	17.283	1.00	21.99
ATOM	1277	C	CYS	368	31.863	39.650	15.106	1.00	23.06
ATOM	1278	O	CYS	368	31.433	38.658	15.699	1.00	21.98
ATOM	1279	N	HIS	369	32.358	39.578	13.877	1.00	23.71
ATOM	1280	CA	HIS	369	32.402	38.291	13.185	1.00	24.68
ATOM	1281	CB	HIS	369	32.429	38.498	11.667	1.00	24.85
ATOM	1282	CG	HIS	369	33.754	38.951	11.138	1.00	27.37
ATOM	1283	CD2	HIS	369	34.644	38.338	10.323	1.00	28.58
ATOM	1284	ND1	HIS	369	34.306	40.175	11.452	1.00	29.21
ATOM	1285	CE1	HIS	369	35.480	40.295	10.859	1.00	29.19
ATOM	1286	NE2	HIS	369	35.708	39.194	10.168	1.00	29.69
ATOM	1287	C	HIS	369	33.550	37.372	13.606	1.00	24.39
ATOM	1288	O	HIS	369	33.440	36.153	13.506	1.00	24.00
ATOM	1289	N	SER	370	34.641	37.959	14.087	1.00	24.30
ATOM	1290	CA	SER	370	35.814	37.189	14.479	1.00	24.06
ATOM	1291	CB	SER	370	36.949	37.460	13.494	1.00	24.57
ATOM	1292	OG	SER	370	37.431	38.784	13.648	1.00	26.06
ATOM	1293	C	SER	370	36.269	37.518	15.892	1.00	23.01
ATOM	1294	O	SER	370	35.936	38.574	16.433	1.00	23.58
ATOM	1295	N	LYS	371	37.076	36.633	16.461	1.00	23.64
ATOM	1296	CA	LYS	371	37.587	36.797	17.817	1.00	25.06
ATOM	1297	CB	LYS	371	38.146	35.466	18.320	1.00	24.91
ATOM	1298	CG	LYS	371	37.086	34.372	18.306	1.00	27.06
ATOM	1299	CD	LYS	371	37.648	32.979	18.078	1.00	28.04
ATOM	1300	CE	LYS	371	38.277	32.415	19.318	1.00	28.77
ATOM	1301	NZ	LYS	371	38.642	30.999	19.107	1.00	31.47
ATOM	1302	C	LYS	371	38.625	37.904	17.877	1.00	25.64
ATOM	1303	O	LYS	371	38.689	38.650	18.849	1.00	27.42
ATOM	1304	N	LYS	372	39.379	38.061	16.795	1.00	27.32
ATOM	1305	CA	LYS	372	40.402	39.100	16.707	1.00	28.80
ATOM	1306	CB	LYS	372	41.136	39.010	15.366	1.00	29.78
ATOM	1307	CG	LYS	372	42.339	39.923	15.243	1.00	30.84
ATOM	1308	CD	LYS	372	42.976	39.812	13.866	1.00	31.69
ATOM	1309	C	LYS	372	39.729	40.455	16.842	1.00	28.53
ATOM	1310	O	LYS	372	40.095	41.255	17.696	1.00	28.67
ATOM	1311	N	LYS	373	38.720	40.688	16.008	1.00	29.86
ATOM	1312	CA	LYS	373	37.966	41.935	16.040	1.00	30.80
ATOM	1313	CB	LYS	373	36.864	41.927	14.975	1.00	32.75
ATOM	1314	CG	LYS	373	37.131	42.879	13.817	1.00	38.26
ATOM	1315	CD	LYS	373	38.427	42.514	13.101	1.00	42.40
ATOM	1316	CE	LYS	373	38.993	43.676	12.295	1.00	43.70
ATOM	1317	NZ	LYS	373	40.324	43.301	11.729	1.00	45.18
ATOM	1318	C	LYS	373	37.362	42.209	17.422	1.00	30.08
ATOM	1319	O	LYS	373	37.301	43.359	17.850	1.00	31.06
ATOM	1320	N	CYS	374	36.923	41.157	18.114	1.00	28.22
ATOM	1321	CA	CYS	374	36.334	41.310	19.438	1.00	26.08
ATOM	1322	CB	CYS	374	35.800	39.970	19.964	1.00	23.42
ATOM	1323	SG	CYS	374	34.336	39.310	19.100	1.00	23.17
ATOM	1324	C	CYS	374	37.402	41.851	20.375	1.00	27.53
ATOM	1325	O	CYS	374	37.162	42.805	21.110	1.00	25.72
ATOM	1326	N	ASP	375	38.588	41.239	20.322	1.00	29.96
ATOM	1327	CA	ASP	375	39.735	41.633	21.149	1.00	31.23
ATOM	1328	CB	ASP	375	40.945	40.739	20.860	1.00	30.10
ATOM	1329	CG	ASP	375	40.737	39.312	21.296	1.00	29.63

ATOM	1330	OD1	ASP	375	39.996	39.076	22.274	1.00	28.42
ATOM	1331	OD2	ASP	375	41.332	38.423	20.657	1.00	30.89
ATOM	1332	C	ASP	375	40.135	43.069	20.861	1.00	31.74
ATOM	1333	O	ASP	375	40.304	43.872	21.783	1.00	33.16
ATOM	1334	N	GLU	376	40.301	43.371	19.577	1.00	31.73
ATOM	1335	CA	GLU	376	40.686	44.701	19.127	1.00	33.34
ATOM	1336	CB	GLU	376	40.848	44.715	17.603	1.00	34.63
ATOM	1337	CG	GLU	376	41.791	43.621	17.095	1.00	38.95
ATOM	1338	CD	GLU	376	42.234	43.797	15.646	1.00	40.85
ATOM	1339	OE1	GLU	376	41.453	44.311	14.813	1.00	42.74
ATOM	1340	OE2	GLU	376	43.380	43.401	15.340	1.00	42.32
ATOM	1341	C	GLU	376	39.696	45.776	19.581	1.00	32.36
ATOM	1342	O	GLU	376	40.099	46.831	20.067	1.00	32.77
ATOM	1343	N	LEU	377	38.404	45.493	19.464	1.00	31.01
ATOM	1344	CA	LEU	377	37.398	46.456	19.871	1.00	29.80
ATOM	1345	CB	LEU	377	36.014	46.042	19.375	1.00	27.58
ATOM	1346	CG	LEU	377	34.886	47.037	19.646	1.00	25.16
ATOM	1347	CD1	LEU	377	35.306	48.433	19.220	1.00	26.04
ATOM	1348	CD2	LEU	377	33.635	46.611	18.901	1.00	24.83
ATOM	1349	C	LEU	377	37.408	46.603	21.384	1.00	31.08
ATOM	1350	O	LEU	377	37.488	47.713	21.908	1.00	32.49
ATOM	1351	N	ALA	378	37.362	45.481	22.089	1.00	31.01
ATOM	1352	CA	ALA	378	37.372	45.516	23.541	1.00	31.90
ATOM	1353	CB	ALA	378	37.518	44.102	24.109	1.00	30.31
ATOM	1354	C	ALA	378	38.532	46.398	23.990	1.00	33.00
ATOM	1355	O	ALA	378	38.350	47.303	24.800	1.00	32.23
ATOM	1356	N	ALA	379	39.703	46.171	23.399	1.00	34.63
ATOM	1357	CA	ALA	379	40.906	46.931	23.725	1.00	36.26
ATOM	1358	CB	ALA	379	42.087	46.423	22.915	1.00	36.36
ATOM	1359	C	ALA	379	40.690	48.416	23.471	1.00	37.24
ATOM	1360	O	ALA	379	40.968	49.243	24.339	1.00	38.17
ATOM	1361	N	LYS	380	40.146	48.741	22.303	1.00	38.24
ATOM	1362	CA	LYS	380	39.880	50.125	21.935	1.00	39.63
ATOM	1363	CB	LYS	380	39.184	50.196	20.565	1.00	39.82
ATOM	1364	CG	LYS	380	39.223	51.577	19.904	1.00	40.69
ATOM	1365	CD	LYS	380	38.828	51.510	18.434	1.00	40.39
ATOM	1366	CE	LYS	380	39.265	52.757	17.654	1.00	41.28
ATOM	1367	NZ	LYS	380	38.608	54.040	18.063	1.00	40.83
ATOM	1368	C	LYS	380	39.005	50.782	22.997	1.00	40.87
ATOM	1369	O	LYS	380	39.405	51.768	23.619	1.00	42.50
ATOM	1370	N	LEU	381	37.843	50.187	23.250	1.00	40.55
ATOM	1371	CA	LEU	381	36.891	50.711	24.226	1.00	40.18
ATOM	1372	CB	LEU	381	35.632	49.842	24.243	1.00	38.99
ATOM	1373	CG	LEU	381	34.870	49.610	22.940	1.00	37.56
ATOM	1374	CD1	LEU	381	33.654	48.758	23.223	1.00	35.03
ATOM	1375	CD2	LEU	381	34.464	50.938	22.331	1.00	38.01
ATOM	1376	C	LEU	381	37.458	50.801	25.642	1.00	40.57
ATOM	1377	O	LEU	381	37.302	51.822	26.323	1.00	39.48
ATOM	1378	N	VAL	382	38.096	49.721	26.083	1.00	42.00
ATOM	1379	CA	VAL	382	38.681	49.650	27.419	1.00	42.99
ATOM	1380	CB	VAL	382	39.322	48.252	27.692	1.00	42.81
ATOM	1381	CG1	VAL	382	40.811	48.255	27.393	1.00	42.57
ATOM	1382	CG2	VAL	382	39.040	47.810	29.113	1.00	40.95
ATOM	1383	C	VAL	382	39.699	50.775	27.575	1.00	44.23
ATOM	1384	O	VAL	382	39.378	51.315	28.670	1.00	45.11
ATOM	1385	N	ALA	383	40.322	51.153	26.462	1.00	44.34
ATOM	1386	CA	ALA	383	41.293	52.244	26.468	1.00	44.39
ATOM	1387	CB	ALA	383	42.115	52.333	25.191	1.00	44.85

ATOM	1388	C	ALA	383	40.556	53.574	26.626	1.00	43.71
ATOM	1389	O	ALA	383	41.035	54.481	27.312	1.00	46.22
ATOM	1390	N	LEU	384	39.378	53.679	26.018	1.00	40.83
ATOM	1391	CA	LEU	384	38.578	54.895	26.099	1.00	38.30
ATOM	1392	CB	LEU	384	37.633	54.988	24.899	1.00	39.47
ATOM	1393	CG	LEU	384	38.227	54.865	23.491	1.00	41.58
ATOM	1394	CD1	LEU	384	37.102	54.745	22.468	1.00	42.20
ATOM	1395	CD2	LEU	384	39.130	56.052	23.168	1.00	42.42
ATOM	1396	C	LEU	384	37.771	54.952	27.404	1.00	36.79
ATOM	1397	O	LEU	384	36.787	55.688	27.505	1.00	36.24
ATOM	1398	N	GLY	385	38.164	54.147	28.385	1.00	35.50
ATOM	1399	CA	GLY	385	37.475	54.145	29.664	1.00	33.80
ATOM	1400	C	GLY	385	36.171	53.364	29.713	1.00	33.33
ATOM	1401	O	GLY	385	35.474	53.391	30.728	1.00	34.28
ATOM	1402	N	ILE	386	35.825	52.668	28.633	1.00	31.60
ATOM	1403	CA	ILE	386	34.590	51.890	28.604	1.00	28.68
ATOM	1404	CB	ILE	386	34.121	51.649	27.152	1.00	27.72
ATOM	1405	CG2	ILE	386	32.933	50.698	27.124	1.00	28.20
ATOM	1406	CG1	ILE	386	33.749	52.967	26.486	1.00	25.89
ATOM	1407	CD1	ILE	386	32.566	53.650	27.126	1.00	27.25
ATOM	1408	C	ILE	386	34.810	50.535	29.282	1.00	28.13
ATOM	1409	O	ILE	386	35.838	49.890	29.061	1.00	26.54
ATOM	1410	N	ASN	387	33.844	50.098	30.092	1.00	27.35
ATOM	1411	CA	ASN	387	33.944	48.800	30.771	1.00	26.98
ATOM	1412	CB	ASN	387	33.020	48.745	31.997	1.00	26.31
ATOM	1413	CG	ASN	387	33.080	47.404	32.715	1.00	26.76
ATOM	1414	OD1	ASN	387	34.130	46.749	32.741	1.00	27.49
ATOM	1415	ND2	ASN	387	31.960	46.993	33.306	1.00	23.98
ATOM	1416	C	ASN	387	33.579	47.697	29.780	1.00	25.60
ATOM	1417	O	ASN	387	32.509	47.090	29.867	1.00	25.99
ATOM	1418	N	ALA	388	34.465	47.470	28.817	1.00	24.50
ATOM	1419	CA	ALA	388	34.241	46.474	27.780	1.00	24.38
ATOM	1420	CB	ALA	388	34.692	47.012	26.430	1.00	20.14
ATOM	1421	C	ALA	388	34.945	45.167	28.088	1.00	24.87
ATOM	1422	O	ALA	388	36.080	45.156	28.559	1.00	27.09
ATOM	1423	N	VAL	389	34.269	44.059	27.829	1.00	25.51
ATOM	1424	CA	VAL	389	34.842	42.750	28.076	1.00	25.75
ATOM	1425	CB	VAL	389	34.277	42.094	29.368	1.00	27.61
ATOM	1426	CG1	VAL	389	34.659	42.918	30.586	1.00	27.58
ATOM	1427	CG2	VAL	389	32.772	41.946	29.293	1.00	30.47
ATOM	1428	C	VAL	389	34.540	41.896	26.873	1.00	24.33
ATOM	1429	O	VAL	389	33.464	41.989	26.300	1.00	24.05
ATOM	1430	N	ALA	390	35.520	41.119	26.444	1.00	25.42
ATOM	1431	CA	ALA	390	35.345	40.253	25.285	1.00	26.04
ATOM	1432	CB	ALA	390	36.674	40.083	24.531	1.00	23.07
ATOM	1433	C	ALA	390	34.794	38.888	25.667	1.00	26.03
ATOM	1434	O	ALA	390	34.959	38.416	26.799	1.00	25.70
ATOM	1435	N	TYR	391	34.076	38.286	24.732	1.00	26.60
ATOM	1436	CA	TYR	391	33.565	36.952	24.940	1.00	26.52
ATOM	1437	CB	TYR	391	32.235	35.903	25.691	1.00	25.87
ATOM	1438	CG	TYR	391	31.857	35.459	25.965	1.00	27.47
ATOM	1439	CD1	TYR	391	32.555	34.713	26.915	1.00	28.87
ATOM	1440	CE1	TYR	391	32.306	33.360	27.087	1.00	29.43
ATOM	1441	CD2	TYR	391	30.886	34.802	25.199	1.00	27.70
ATOM	1442	CE2	TYR	391	30.630	33.445	25.368	1.00	26.82
ATOM	1443	CZ	TYR	391	31.344	32.737	26.310	1.00	28.58
ATOM	1444	OH	TYR	391	31.097	31.405	26.511	1.00	30.59
ATOM	1445	C	TYR	391	33.422	36.195	23.645	1.00	26.74

ATOM	1446	O	TYR	391	32.853	36.685	22.675	1.00	25.62
ATOM	1447	N	TYR	392	33.981	34.997	23.646	1.00	28.03
ATOM	1448	CA	TYR	392	33.906	34.095	22.522	1.00	30.93
ATOM	1449	CB	TYR	392	34.803	34.551	21.377	1.00	31.00
ATOM	1450	CG	TYR	392	36.167	35.043	21.778	1.00	30.91
ATOM	1451	CD1	TYR	392	37.158	34.157	22.202	1.00	30.94
ATOM	1452	CE1	TYR	392	38.436	34.609	22.509	1.00	29.59
ATOM	1453	CD2	TYR	392	36.492	36.394	21.678	1.00	29.43
ATOM	1454	CE2	TYR	392	37.757	36.846	21.982	1.00	29.05
ATOM	1455	CZ	TYR	392	38.720	35.949	22.396	1.00	27.90
ATOM	1456	OH	TYR	392	39.964	36.401	22.718	1.00	29.68
ATOM	1457	C	TYR	392	34.262	32.706	23.026	1.00	33.17
ATOM	1458	O	TYR	392	34.577	32.547	24.204	1.00	33.99
ATOM	1459	N	ARG	393	34.163	31.706	22.154	1.00	35.69
ATOM	1460	CA	ARG	393	34.450	30.324	22.528	1.00	36.12
ATOM	1461	CB	ARG	393	34.221	29.383	21.344	1.00	40.66
ATOM	1462	CG	ARG	393	34.624	27.931	21.595	1.00	45.96
ATOM	1463	CD	ARG	393	34.246	27.040	20.406	1.00	50.06
ATOM	1464	NE	ARG	393	32.903	26.481	20.602	1.00	53.83
ATOM	1465	CZ	ARG	393	32.668	25.370	21.300	1.00	55.97
ATOM	1466	NH1	ARG	393	31.415	24.957	21.475	1.00	57.63
ATOM	1467	NH2	ARG	393	33.682	24.619	21.738	1.00	57.66
ATOM	1468	C	ARG	393	35.862	30.178	23.071	1.00	34.84
ATOM	1469	O	ARG	393	36.833	30.615	22.448	1.00	33.70
ATOM	1470	N	GLY	394	35.946	29.572	24.253	1.00	33.32
ATOM	1471	CA	GLY	394	37.211	29.374	24.929	1.00	32.50
ATOM	1472	C	GLY	394	37.360	30.280	26.141	1.00	31.93
ATOM	1473	O	GLY	394	38.203	30.031	27.005	1.00	33.23
ATOM	1474	N	LEU	395	36.552	31.336	26.205	1.00	30.71
ATOM	1475	CA	LEU	395	36.601	32.281	27.317	1.00	29.49
ATOM	1476	CB	LEU	395	36.238	33.695	26.869	1.00	26.83
ATOM	1477	CG	LEU	395	37.160	34.324	25.830	1.00	25.83
ATOM	1478	CD1	LEU	395	37.126	35.822	26.000	1.00	25.35
ATOM	1479	CD2	LEU	395	38.586	33.824	25.988	1.00	25.20
ATOM	1480	C	LEU	395	35.712	31.868	28.470	1.00	29.64
ATOM	1481	O	LEU	395	35.046	30.833	28.415	1.00	30.33
ATOM	1482	N	ASP	396	35.700	32.691	29.510	1.00	30.84
ATOM	1483	CA	ASP	396	34.912	32.411	30.697	1.00	32.76
ATOM	1484	CB	ASP	396	35.813	32.527	31.936	1.00	33.42
ATOM	1485	CG	ASP	396	35.194	31.932	33.187	1.00	32.63
ATOM	1486	OD1	ASP	396	33.996	31.567	33.191	1.00	32.81
ATOM	1487	OD2	ASP	396	35.932	31.823	34.180	1.00	34.06
ATOM	1488	C	ASP	396	33.731	33.376	30.790	1.00	33.30
ATOM	1489	O	ASP	396	33.900	34.569	31.070	1.00	33.42
ATOM	1490	N	VAL	397	32.529	32.842	30.605	1.00	33.00
ATOM	1491	CA	VAL	397	31.327	33.653	30.650	1.00	33.17
ATOM	1492	CB	VAL	397	30.145	32.937	29.985	1.00	34.45
ATOM	1493	CG1	VAL	397	29.616	31.827	30.898	1.00	34.59
ATOM	1494	CG2	VAL	397	29.052	33.945	29.604	1.00	33.81
ATOM	1495	C	VAL	397	30.913	34.130	32.047	1.00	32.83
ATOM	1496	O	VAL	397	30.157	35.099	32.176	1.00	33.92
ATOM	1497	N	SER	398	31.419	33.478	33.089	1.00	31.23
ATOM	1498	CA	SER	398	31.060	33.865	34.445	1.00	30.65
ATOM	1499	CB	SER	398	31.390	32.741	35.424	1.00	31.52
ATOM	1500	OG	SER	398	32.755	32.370	35.345	1.00	33.10
ATOM	1501	C	SER	398	31.714	35.166	34.910	1.00	30.89
ATOM	1502	O	SER	398	31.368	35.700	35.966	1.00	31.97
ATOM	1503	N	VAL	399	30.668	35.673	34.140	1.00	30.43

ATOM	1504	CA	VAL	399	33.326	36.907	34.529	1.00	29.65
ATOM	1505	CB	VAL	399	34.793	36.976	34.008	1.00	29.94
ATOM	1506	CG1	VAL	399	35.501	35.636	34.242	1.00	29.09
ATOM	1507	CG2	VAL	399	34.841	37.372	32.552	1.00	29.84
ATOM	1508	C	VAL	399	32.512	38.122	34.076	1.00	29.51
ATOM	1509	O	VAL	399	32.753	39.245	34.530	1.00	30.22
ATOM	1510	N	ILE	400	31.534	37.889	33.202	1.00	27.63
ATOM	1511	CA	ILE	400	30.682	38.961	32.695	1.00	26.65
ATOM	1512	CB	ILE	400	29.877	38.489	31.457	1.00	26.73
ATOM	1513	CG2	ILE	400	29.017	39.627	30.912	1.00	24.30
ATOM	1514	CG1	ILE	400	30.836	37.966	30.381	1.00	27.93
ATOM	1515	CD1	ILE	400	30.161	37.431	29.132	1.00	27.24
ATOM	1516	C	ILE	400	29.717	39.357	33.808	1.00	26.54
ATOM	1517	O	ILE	400	28.987	38.521	34.320	1.00	25.84
ATOM	1518	N	PRO	401	29.720	40.637	34.213	1.00	27.05
ATOM	1519	CD	PRO	401	30.441	41.786	33.632	1.00	26.21
ATOM	1520	CA	PRO	401	28.816	41.069	35.281	1.00	27.20
ATOM	1521	CB	PRO	401	29.191	42.537	35.469	1.00	26.22
ATOM	1522	CG	PRO	401	29.597	42.959	34.085	1.00	25.90
ATOM	1523	C	PRO	401	27.339	40.903	34.906	1.00	29.40
ATOM	1524	O	PRO	401	26.945	41.134	33.773	1.00	29.57
ATOM	1525	N	THR	402	26.551	40.447	35.871	1.00	30.54
ATOM	1526	CA	THR	402	25.123	40.231	35.727	1.00	30.29
ATOM	1527	CB	THR	402	24.663	39.255	36.825	1.00	31.76
ATOM	1528	OG1	THR	402	25.063	37.929	36.462	1.00	35.36
ATOM	1529	CG2	THR	402	23.168	39.308	37.059	1.00	34.23
ATOM	1530	C	THR	402	24.373	41.557	35.835	1.00	29.90
ATOM	1531	O	THR	402	23.246	41.695	35.357	1.00	29.95
ATOM	1532	N	SER	403	24.997	42.532	36.474	1.00	29.98
ATOM	1533	CA	SER	403	24.385	43.839	36.624	1.00	30.57
ATOM	1534	CB	SER	403	23.655	43.927	37.961	1.00	30.45
ATOM	1535	OG	SER	403	24.372	43.219	38.954	1.00	34.50
ATOM	1536	C	SER	403	25.451	44.917	36.499	1.00	30.16
ATOM	1537	O	SER	403	26.650	44.628	36.581	1.00	30.53
ATOM	1538	N	GLY	404	25.008	46.146	36.265	1.00	29.14
ATOM	1539	CA	GLY	404	25.924	47.257	36.119	1.00	27.59
ATOM	1540	C	GLY	404	26.336	47.472	34.675	1.00	26.53
ATOM	1541	O	GLY	404	26.237	46.563	33.852	1.00	26.16
ATOM	1542	N	ASP	405	26.796	48.685	34.381	1.00	25.54
ATOM	1543	CA	ASP	405	27.241	49.067	33.049	1.00	23.74
ATOM	1544	CB	ASP	405	27.837	50.468	33.062	1.00	23.03
ATOM	1545	CG	ASP	405	26.838	51.530	33.392	1.00	24.18
ATOM	1546	OD1	ASP	405	25.636	51.217	33.568	1.00	22.99
ATOM	1547	OD2	ASP	405	27.277	52.698	33.480	1.00	24.90
ATOM	1548	C	ASP	405	28.324	48.156	32.543	1.00	23.67
ATOM	1549	O	ASP	405	29.292	47.873	33.259	1.00	25.75
ATOM	1550	N	VAL	406	28.211	47.774	31.279	1.00	23.25
ATOM	1551	CA	VAL	406	29.210	46.926	30.656	1.00	22.78
ATOM	1552	CB	VAL	406	29.259	45.506	31.291	1.00	23.65
ATOM	1553	CG1	VAL	406	27.978	44.730	30.983	1.00	25.24
ATOM	1554	CG2	VAL	406	30.505	44.741	30.809	1.00	23.18
ATOM	1555	C	VAL	406	28.916	46.807	29.131	1.00	21.61
ATOM	1556	O	VAL	406	27.767	46.920	28.760	1.00	23.02
ATOM	1557	N	VAL	407	29.973	46.672	28.392	1.00	20.23
ATOM	1558	CA	VAL	407	29.842	46.490	26.960	1.00	17.52
ATOM	1559	CB	VAL	407	30.487	47.639	26.159	1.00	15.18
ATOM	1560	CG1	VAL	407	30.314	47.406	24.675	1.00	11.58
ATOM	1561	CG2	VAL	407	29.852	48.966	26.549	1.00	15.21

ATOM	1562	C	VAL	407	30.548	45.178	26.659	1.00	17.42
ATOM	1563	O	VAL	407	31.753	45.060	26.806	1.00	18.03
ATOM	1564	N	VAL	408	29.773	44.155	26.351	1.00	17.67
ATOM	1565	CA	VAL	408	30.340	42.868	26.025	1.00	18.23
ATOM	1566	CB	VAL	408	29.371	41.733	26.449	1.00	19.02
ATOM	1567	CG1	VAL	408	29.885	40.373	26.012	1.00	18.33
ATOM	1568	CG2	VAL	408	29.178	41.757	27.947	1.00	17.66
ATOM	1569	C	VAL	408	30.572	42.860	24.509	1.00	18.78
ATOM	1570	O	VAL	408	29.686	43.231	23.742	1.00	18.45
ATOM	1571	N	VAL	409	31.800	42.568	24.093	1.00	17.88
ATOM	1572	CA	VAL	409	32.137	42.483	22.679	1.00	17.88
ATOM	1573	CB	VAL	409	33.418	43.249	22.359	1.00	17.72
ATOM	1574	CG1	VAL	409	33.718	43.135	20.884	1.00	19.24
ATOM	1575	CG2	VAL	409	33.264	44.719	22.749	1.00	17.08
ATOM	1576	C	VAL	409	32.308	40.978	22.435	1.00	18.24
ATOM	1577	O	VAL	409	33.267	40.360	22.909	1.00	16.84
ATOM	1578	N	ALA	410	31.392	40.397	21.668	1.00	18.77
ATOM	1579	CA	ALA	410	31.400	38.958	21.473	1.00	18.14
ATOM	1580	CB	ALA	410	30.431	38.351	22.486	1.00	18.34
ATOM	1581	C	ALA	410	31.054	38.426	20.089	1.00	17.88
ATOM	1582	O	ALA	410	30.686	39.176	19.181	1.00	18.45
ATOM	1583	N	THR	411	31.194	37.109	19.950	1.00	16.99
ATOM	1584	CA	THR	411	30.827	36.404	18.738	1.00	17.24
ATOM	1585	CB	THR	411	31.821	35.299	18.361	1.00	16.51
ATOM	1586	OG1	THR	411	31.863	34.331	19.409	1.00	18.59
ATOM	1587	CG2	THR	411	33.204	35.852	18.101	1.00	18.00
ATOM	1588	C	THR	411	29.504	35.711	19.103	1.00	19.33
ATOM	1589	O	THR	411	28.972	35.889	20.204	1.00	20.25
ATOM	1590	N	ASP	412	29.016	34.851	18.221	1.00	21.45
ATOM	1591	CA	ASP	412	27.768	34.145	18.473	1.00	22.15
ATOM	1592	CB	ASP	412	27.239	33.567	17.166	1.00	19.65
ATOM	1593	CG	ASP	412	26.783	34.635	16.221	1.00	15.73
ATOM	1594	OD1	ASP	412	26.071	35.534	16.684	1.00	16.40
ATOM	1595	OD2	ASP	412	27.137	34.591	15.031	1.00	16.44
ATOM	1596	C	ASP	412	27.868	33.064	19.549	1.00	24.32
ATOM	1597	O	ASP	412	26.888	32.380	19.848	1.00	23.10
ATOM	1598	N	ALA	413	29.055	32.920	20.125	1.00	28.20
ATOM	1599	CA	ALA	413	29.284	31.937	21.168	1.00	31.95
ATOM	1600	CB	ALA	413	30.724	31.974	21.611	1.00	31.34
ATOM	1601	C	ALA	413	28.371	32.172	22.360	1.00	35.40
ATOM	1602	O	ALA	413	27.812	31.222	22.905	1.00	38.88
ATOM	1603	N	LEU	414	28.207	33.434	22.755	1.00	38.48
ATOM	1604	CA	LEU	414	27.368	33.772	23.911	1.00	40.49
ATOM	1605	CB	LEU	414	27.411	35.292	24.203	1.00	40.58
ATOM	1606	CG	LEU	414	26.880	35.779	25.570	1.00	39.61
ATOM	1607	CD1	LEU	414	27.734	35.225	26.691	1.00	39.02
ATOM	1608	CD2	LEU	414	26.855	37.290	25.652	1.00	38.26
ATOM	1609	C	LEU	414	25.923	33.298	23.721	1.00	41.04
ATOM	1610	O	LEU	414	25.586	32.245	24.309	1.00	41.21
ATOM	1611	CB	PHE	418	23.962	34.889	28.719	1.00	49.92
ATOM	1612	CG	PHE	418	24.665	35.936	29.554	1.00	49.95
ATOM	1613	CD1	PHE	418	25.107	35.639	30.844	1.00	48.64
ATOM	1614	CD2	PHE	418	24.847	37.228	29.063	1.00	49.25
ATOM	1615	CE1	PHE	418	25.716	36.613	31.632	1.00	48.52
ATOM	1616	CE2	PHE	418	25.457	38.212	29.846	1.00	49.33
ATOM	1617	CZ	PHE	418	25.890	37.905	31.131	1.00	48.87
ATOM	1618	C	PHE	418	21.732	35.511	29.710	1.00	48.72
ATOM	1619	O	PHE	418	21.041	36.066	28.842	1.00	48.37

ATOM	1620	N	PHE	418	22.021	33.365	28.442	1.00	50.78
ATOM	1621	CA	PHE	418	22.670	34.351	29.353	1.00	49.76
ATOM	1622	N	THR	419	21.697	35.856	30.994	1.00	46.61
ATOM	1623	CA	THR	419	20.872	36.956	31.471	1.00	45.71
ATOM	1624	CB	THR	419	20.577	36.801	32.970	1.00	48.47
ATOM	1625	OG1	THR	419	21.767	36.364	33.654	1.00	51.07
ATOM	1626	CG2	THR	419	19.463	35.785	33.182	1.00	48.87
ATOM	1627	C	THR	419	21.628	38.257	31.213	1.00	43.14
ATOM	1628	O	THR	419	22.191	38.865	32.124	1.00	42.27
ATOM	1629	N	GLY	420	21.651	38.662	29.950	1.00	41.16
ATOM	1630	CA	GLY	420	22.362	39.862	29.568	1.00	37.36
ATOM	1631	C	GLY	420	21.732	41.160	30.017	1.00	35.27
ATOM	1632	O	GLY	420	22.436	42.091	30.376	1.00	34.05
ATOM	1633	N	ASP	421	20.407	41.238	29.972	1.00	34.00
ATOM	1634	CA	ASP	421	19.705	42.454	30.365	1.00	31.58
ATOM	1635	CB	ASP	421	19.751	42.629	31.886	1.00	33.33
ATOM	1636	CG	ASP	421	18.986	43.842	32.350	1.00	36.90
ATOM	1637	OD1	ASP	421	17.869	44.063	31.838	1.00	37.58
ATOM	1638	OD2	ASP	421	19.510	44.586	33.212	1.00	39.50
ATOM	1639	C	ASP	421	20.376	43.626	29.654	1.00	29.23
ATOM	1640	O	ASP	421	20.784	44.614	30.274	1.00	27.56
ATOM	1641	N	PHE	422	20.510	43.480	28.340	1.00	27.41
ATOM	1642	CA	PHE	422	21.148	44.485	27.495	1.00	25.64
ATOM	1643	CB	PHE	422	21.792	43.818	26.269	1.00	21.10
ATOM	1644	CG	PHE	422	22.973	42.955	26.601	1.00	17.18
ATOM	1645	CD1	PHE	422	22.951	41.595	26.328	1.00	14.50
ATOM	1646	CD2	PHE	422	24.111	43.504	27.190	1.00	15.37
ATOM	1647	CE1	PHE	422	24.049	40.787	26.638	1.00	14.66
ATOM	1648	CE2	PHE	422	25.214	42.711	27.503	1.00	14.24
ATOM	1649	CZ	PHE	422	25.185	41.353	27.229	1.00	12.70
ATOM	1650	C	PHE	422	20.236	45.626	27.044	1.00	24.93
ATOM	1651	O	PHE	422	19.110	45.409	26.605	1.00	24.73
ATOM	1652	N	ASP	423	20.740	46.846	27.167	1.00	24.37
ATOM	1653	CA	ASP	423	20.010	48.033	26.752	1.00	24.05
ATOM	1654	CB	ASP	423	20.607	49.285	27.398	1.00	24.07
ATOM	1655	CG	ASP	423	20.341	49.339	28.870	1.00	23.88
ATOM	1656	OD1	ASP	423	19.159	49.417	29.246	1.00	27.21
ATOM	1657	OD2	ASP	423	21.294	49.268	29.658	1.00	24.16
ATOM	1658	C	ASP	423	20.048	48.147	25.239	1.00	23.57
ATOM	1659	O	ASP	423	19.154	48.747	24.638	1.00	23.30
ATOM	1660	N	SER	424	21.086	47.585	24.626	1.00	21.30
ATOM	1661	CA	SER	424	21.182	47.611	23.182	1.00	20.49
ATOM	1662	CB	SER	424	21.644	48.981	22.691	1.00	21.66
ATOM	1663	OG	SER	424	23.054	49.075	22.716	1.00	22.36
ATOM	1664	C	SER	424	22.110	46.538	22.633	1.00	20.13
ATOM	1665	O	SER	424	22.919	45.950	23.369	1.00	18.98
ATOM	1666	N	VAL	425	21.940	46.272	21.339	1.00	18.97
ATOM	1667	CA	VAL	425	22.751	45.319	20.588	1.00	16.27
ATOM	1668	CB	VAL	425	21.916	44.095	20.052	1.00	15.46
ATOM	1669	CG1	VAL	425	22.703	43.332	18.999	1.00	12.48
ATOM	1670	CG2	VAL	425	21.560	43.148	21.177	1.00	11.79
ATOM	1671	C	VAL	425	23.259	46.094	19.332	1.00	15.96
ATOM	1672	O	VAL	425	22.501	46.848	18.767	1.00	15.96
ATOM	1673	N	ILE	426	24.556	46.003	19.115	1.00	15.81
ATOM	1674	CA	ILE	426	25.139	46.644	17.947	1.00	16.74
ATOM	1675	CB	ILE	426	26.251	47.640	18.304	1.00	18.60
ATOM	1676	CG2	ILE	426	26.805	48.275	17.022	1.00	18.26
ATOM	1677	CG1	ILE	426	25.697	48.710	19.254	1.00	17.67

ATOM	1678	CD1	ILE	426	26.635	49.857	19.531	1.00	19.38
ATOM	1679	C	ILE	426	25.669	45.434	17.199	1.00	17.81
ATOM	1680	O	ILE	426	26.385	44.611	17.774	1.00	18.67
ATOM	1681	N	ASP	427	25.295	45.318	15.931	1.00	18.83
ATOM	1682	CA	ASP	427	25.625	44.158	15.110	1.00	18.61
ATOM	1683	CB	ASP	427	24.284	43.525	14.711	1.00	19.39
ATOM	1684	CG	ASP	427	24.405	42.146	14.094	1.00	18.80
ATOM	1685	OD1	ASP	427	25.516	41.611	13.922	1.00	17.99
ATOM	1686	OD2	ASP	427	23.337	41.592	13.774	1.00	19.23
ATOM	1687	C	ASP	427	26.417	44.516	13.870	1.00	18.42
ATOM	1688	O	ASP	427	26.077	45.479	13.185	1.00	19.02
ATOM	1689	N	CYS	428	27.454	43.728	13.570	1.00	17.93
ATOM	1690	CA	CYS	428	28.277	43.944	12.375	1.00	18.18
ATOM	1691	CB	CYS	428	29.628	43.247	12.502	1.00	18.00
ATOM	1692	SG	CYS	428	29.549	41.453	12.475	1.00	19.71
ATOM	1693	C	CYS	428	27.555	43.423	11.135	1.00	18.32
ATOM	1694	O	CYS	428	27.944	43.708	10.011	1.00	21.01
ATOM	1695	N	ASN	429	26.530	42.609	11.351	1.00	18.21
ATOM	1696	CA	ASN	429	25.713	42.055	10.272	1.00	18.70
ATOM	1697	CB	ASN	429	25.054	43.180	9.462	1.00	18.15
ATOM	1698	CG	ASN	429	24.271	44.152	10.336	1.00	18.71
ATOM	1699	OD1	ASN	429	24.504	45.356	10.294	1.00	19.89
ATOM	1700	ND2	ASN	429	23.358	43.633	11.147	1.00	17.96
ATOM	1701	C	ASN	429	26.386	41.043	9.352	1.00	18.76
ATOM	1702	O	ASN	429	25.867	40.732	8.283	1.00	18.71
ATOM	1703	N	THR	430	27.517	40.492	9.781	1.00	19.72
ATOM	1704	CA	THR	430	28.226	39.486	8.996	1.00	19.58
ATOM	1705	CB	THR	430	29.527	40.044	8.377	1.00	18.32
ATOM	1706	OG1	THR	430	30.433	40.441	9.413	1.00	18.44
ATOM	1707	CG2	THR	430	29.215	41.241	7.505	1.00	16.13
ATOM	1708	C	THR	430	28.532	38.291	9.893	1.00	20.27
ATOM	1709	O	THR	430	28.475	38.399	11.112	1.00	20.61
ATOM	1710	N	CME	431	28.829	37.144	9.300	1.00	21.71
ATOM	1711	CA	CME	431	29.118	35.958	10.088	1.00	23.49
ATOM	1712	C	CME	431	30.100	35.064	9.351	1.00	23.26
ATOM	1713	O	CME	431	30.117	35.024	8.124	1.00	24.03
ATOM	1714	CB	CME	431	27.822	35.191	10.390	1.00	24.65
ATOM	1715	SG	CME	431	26.882	34.701	8.908	1.00	28.78
ATOM	1716	2SG	CME	431	25.080	34.061	9.615	1.00	30.80
ATOM	1717	2CB	CME	431	25.261	32.249	9.685	1.00	32.16
ATOM	1718	2CA	CME	431	26.230	31.721	10.742	1.00	34.08
ATOM	1719	OG	CME	431	26.088	32.402	11.978	1.00	36.06
ATOM	1720	N	VAL	432	30.949	34.393	10.112	1.00	23.66
ATOM	1721	CA	VAL	432	31.952	33.489	9.569	1.00	25.04
ATOM	1722	CB	VAL	432	33.212	33.429	10.487	1.00	26.14
ATOM	1723	CG1	VAL	432	34.215	32.412	9.968	1.00	25.89
ATOM	1724	CG2	VAL	432	33.860	34.811	10.587	1.00	26.03
ATOM	1725	C	VAL	432	31.295	32.135	9.552	1.00	24.44
ATOM	1726	O	VAL	432	30.594	31.730	10.493	1.00	24.47
ATOM	1727	N	THR	433	31.486	31.390	8.474	1.00	25.86
ATOM	1728	CA	THR	433	30.890	30.062	8.374	1.00	26.89
ATOM	1729	CB	THR	433	29.443	30.140	7.829	1.00	26.52
ATOM	1730	OG1	THR	433	28.812	28.859	7.968	1.00	28.69
ATOM	1731	CG2	THR	433	29.438	30.564	6.362	1.00	24.41
ATOM	1732	C	THR	433	31.718	29.093	7.527	1.00	26.04
ATOM	1733	O	THR	433	32.543	29.504	6.709	1.00	24.26
ATOM	1734	N	GLN	434	31.519	27.802	7.774	1.00	27.85
ATOM	1735	CA	GLN	434	32.221	26.750	7.052	1.00	28.61

ATOM	1736	CB	GLN	434	32.034	25.402	7.745	1.00	31.09
ATOM	1737	CG	GLN	434	32.787	25.245	9.044	1.00	35.42
ATOM	1738	CD	GLN	434	34.249	24.893	8.853	1.00	37.94
ATOM	1739	OE1	GLN	434	34.643	23.759	9.081	1.00	44.05
ATOM	1740	NE2	GLN	434	35.057	25.853	8.428	1.00	37.21
ATOM	1741	C	GLN	434	31.701	26.657	5.628	1.00	27.68
ATOM	1742	O	GLN	434	30.494	26.673	5.387	1.00	26.87
ATOM	1743	N	THR	435	32.619	26.503	4.692	1.00	26.85
ATOM	1744	CA	THR	435	32.246	26.416	3.305	1.00	27.23
ATOM	1745	CB	THR	435	32.334	27.804	2.651	1.00	29.34
ATOM	1746	OG1	THR	435	31.794	27.751	1.323	1.00	33.86
ATOM	1747	CG2	THR	435	33.792	28.265	2.593	1.00	29.75
ATOM	1748	C	THR	435	33.184	25.433	2.609	1.00	25.74
ATOM	1749	O	THR	435	34.350	25.287	3.001	1.00	24.92
ATOM	1750	N	VAL	436	32.658	24.734	1.608	1.00	23.49
ATOM	1751	CA	VAL	436	33.447	23.774	0.858	1.00	22.57
ATOM	1752	CB	VAL	436	32.712	22.391	0.684	1.00	21.11
ATOM	1753	CG1	VAL	436	31.389	22.557	-0.029	1.00	19.30
ATOM	1754	CG2	VAL	436	33.602	21.399	-0.061	1.00	17.28
ATOM	1755	C	VAL	436	33.800	24.370	-0.493	1.00	22.79
ATOM	1756	O	VAL	436	33.029	25.129	-1.071	1.00	23.69
ATOM	1757	N	ASP	437	35.009	24.084	-0.951	1.00	23.38
ATOM	1758	CA	ASP	437	35.470	24.562	-2.237	1.00	23.03
ATOM	1759	CB	ASP	437	36.593	25.582	-2.043	1.00	25.16
ATOM	1760	CG	ASP	437	37.087	26.176	-3.358	1.00	27.57
ATOM	1761	OD1	ASP	437	36.421	26.006	-4.408	1.00	28.15
ATOM	1762	OD2	ASP	437	38.156	26.820	-3.332	1.00	30.89
ATOM	1763	C	ASP	437	35.976	23.344	-2.991	1.00	22.31
ATOM	1764	O	ASP	437	36.949	22.724	-2.581	1.00	23.36
ATOM	1765	N	PHE	438	35.257	22.948	-4.031	1.00	22.10
ATOM	1766	CA	PHE	438	35.646	21.804	-4.849	1.00	24.52
ATOM	1767	CB	PHE	438	34.444	21.329	-5.676	1.00	24.50
ATOM	1768	CG	PHE	438	33.252	20.944	-4.833	1.00	27.22
ATOM	1769	CD1	PHE	438	32.162	21.800	-4.713	1.00	27.14
ATOM	1770	CD2	PHE	438	33.242	19.739	-4.123	1.00	27.35
ATOM	1771	CE1	PHE	438	31.079	21.466	-3.897	1.00	27.93
ATOM	1772	CE2	PHE	438	32.166	19.394	-3.305	1.00	26.72
ATOM	1773	CZ	PHE	438	31.084	20.257	-3.191	1.00	28.20
ATOM	1774	C	PHE	438	36.784	22.298	-5.741	1.00	25.20
ATOM	1775	O	PHE	438	36.655	22.372	-6.964	1.00	27.05
ATOM	1776	N	SER	439	37.905	22.609	-5.094	1.00	25.29
ATOM	1777	CA	SER	439	39.087	23.167	-5.732	1.00	24.15
ATOM	1778	CB	SER	439	39.928	23.886	-4.682	1.00	24.18
ATOM	1779	OG	SER	439	39.975	23.146	-3.471	1.00	24.29
ATOM	1780	C	SER	439	39.978	22.302	-6.614	1.00	24.46
ATOM	1781	O	SER	439	40.881	22.834	-7.266	1.00	24.35
ATOM	1782	N	LEU	440	39.766	20.988	-6.615	1.00	24.35
ATOM	1783	CA	LEU	440	40.553	20.083	-7.460	1.00	26.08
ATOM	1784	CB	LEU	440	40.122	20.254	-8.923	1.00	25.16
ATOM	1785	CG	LEU	440	38.607	20.230	-9.120	1.00	26.05
ATOM	1786	CD1	LEU	440	38.242	20.519	-10.563	1.00	25.63
ATOM	1787	CD2	LEU	440	38.072	18.879	-8.673	1.00	26.91
ATOM	1788	C	LEU	440	42.069	20.314	-7.341	1.00	26.71
ATOM	1789	O	LEU	440	42.786	20.331	-8.341	1.00	28.25
ATOM	1790	N	ASP	441	42.551	20.455	-6.111	1.00	26.91
ATOM	1791	CA	ASP	441	43.966	20.705	-5.858	1.00	25.13
ATOM	1792	CB	ASP	441	44.167	22.197	-5.573	1.00	25.06
ATOM	1793	CG	ASP	441	43.347	22.691	-4.367	1.00	27.62

ATOM	1794	OD1	ASP	441	42.462	21.954	-3.863	1.00	26.35
ATOM	1795	OD2	ASP	441	43.605	23.821	-3.905	1.00	26.72
ATOM	1796	C	ASP	441	44.471	19.883	-4.669	1.00	24.82
ATOM	1797	O	ASP	441	45.123	20.420	-3.781	1.00	24.32
ATOM	1798	N	PRO	442	44.328	18.548	-4.718	1.00	24.11
ATOM	1799	CD	PRO	442	44.909	17.709	-3.650	1.00	23.78
ATOM	1800	CA	PRO	442	43.750	17.712	-5.773	1.00	24.26
ATOM	1801	CB	PRO	442	44.505	16.401	-5.588	1.00	23.48
ATOM	1802	CG	PRO	442	44.562	16.289	-4.100	1.00	23.95
ATOM	1803	C	PRO	442	42.250	17.450	-5.747	1.00	24.59
ATOM	1804	O	PRO	442	41.674	17.082	-6.778	1.00	26.09
ATOM	1805	N	THR	443	41.608	17.664	-4.601	1.00	25.49
ATOM	1806	CA	THR	443	40.183	17.360	-4.465	1.00	23.89
ATOM	1807	CB	THR	443	40.014	16.138	-3.532	1.00	23.42
ATOM	1808	OG1	THR	443	40.674	16.405	-2.291	1.00	24.59
ATOM	1809	CG2	THR	443	40.643	14.905	-4.145	1.00	22.83
ATOM	1810	C	THR	443	39.269	18.502	-3.996	1.00	23.35
ATOM	1811	O	THR	443	38.669	19.197	-4.818	1.00	22.91
ATOM	1812	N	PHE	444	39.125	18.666	-2.684	1.00	22.01
ATOM	1813	CA	PHE	444	38.271	19.713	-2.141	1.00	21.72
ATOM	1814	CB	PHE	444	36.883	19.159	-1.748	1.00	20.61
ATOM	1815	CG	PHE	444	36.910	18.077	-0.693	1.00	18.78
ATOM	1816	CD1	PHE	444	36.849	18.399	0.659	1.00	19.13
ATOM	1817	CD2	PHE	444	36.954	16.731	-1.053	1.00	18.82
ATOM	1818	CE1	PHE	444	36.827	17.394	1.640	1.00	18.38
ATOM	1819	CE2	PHE	444	36.933	15.723	-0.081	1.00	16.79
ATOM	1820	CZ	PHE	444	36.869	16.052	1.261	1.00	16.58
ATOM	1821	C	PHE	444	38.931	20.432	-0.971	1.00	21.99
ATOM	1822	O	PHE	444	39.983	19.998	-0.481	1.00	22.62
ATOM	1823	N	THR	445	38.333	21.548	-0.558	1.00	22.06
ATOM	1824	CA	THR	445	38.834	22.353	0.552	1.00	22.10
ATOM	1825	CB	THR	445	39.519	23.642	0.040	1.00	22.17
ATOM	1826	OG1	THR	445	40.542	23.311	-0.903	1.00	24.33
ATOM	1827	CG2	THR	445	40.132	24.423	1.187	1.00	20.65
ATOM	1828	C	THR	445	37.682	22.795	1.452	1.00	21.98
ATOM	1829	O	THR	445	36.674	23.298	0.971	1.00	21.81
ATOM	1830	N	ILE	446	37.806	22.555	2.745	1.00	23.22
ATOM	1831	CA	ILE	446	36.789	22.998	3.684	1.00	26.55
ATOM	1832	CB	ILE	446	36.318	21.874	4.652	1.00	25.92
ATOM	1833	CG2	ILE	446	35.603	22.461	5.858	1.00	25.60
ATOM	1834	CG1	ILE	446	35.346	20.939	3.929	1.00	22.35
ATOM	1835	CD1	ILE	446	35.814	19.552	3.909	1.00	21.01
ATOM	1836	C	ILE	446	37.474	24.125	4.437	1.00	28.48
ATOM	1837	O	ILE	446	38.516	23.921	5.065	1.00	30.14
ATOM	1838	N	GLU	447	36.943	25.330	4.276	1.00	29.02
ATOM	1839	CA	GLU	447	37.494	26.509	4.916	1.00	28.87
ATOM	1840	CB	GLU	447	38.245	27.325	3.867	1.00	29.79
ATOM	1841	CG	GLU	447	37.433	27.601	2.611	1.00	31.68
ATOM	1842	CD	GLU	447	38.282	28.042	1.435	1.00	33.86
ATOM	1843	OE1	GLU	447	39.496	28.280	1.609	1.00	35.31
ATOM	1844	OE2	GLU	447	37.733	28.133	0.317	1.00	37.54
ATOM	1845	C	GLU	447	36.340	27.310	5.520	1.00	29.27
ATOM	1846	O	GLU	447	35.330	26.731	5.919	1.00	29.04
ATOM	1847	N	THR	448	36.497	28.625	5.633	1.00	28.51
ATOM	1848	CA	THR	448	35.431	29.453	6.167	1.00	29.44
ATOM	1849	CB	THR	448	35.720	29.947	7.595	1.00	29.38
ATOM	1850	OG1	THR	448	36.836	30.841	7.584	1.00	30.76
ATOM	1851	CG2	THR	448	36.019	28.797	8.514	1.00	30.09

ATOM	1852	C	THR	448	35.267	30.657	5.261	1.00	29.41
ATOM	1853	O	THR	448	36.198	31.027	4.549	1.00	29.33
ATOM	1854	N	THR	449	34.059	31.213	5.228	1.00	29.92
ATOM	1855	CA	THR	449	33.773	32.390	4.421	1.00	29.42
ATOM	1856	CB	THR	449	32.943	32.047	3.174	1.00	28.46
ATOM	1857	OG1	THR	449	33.623	31.047	2.417	1.00	29.99
ATOM	1858	CG2	THR	449	32.770	33.272	2.294	1.00	28.99
ATOM	1859	C	THR	449	32.976	33.363	5.276	1.00	29.18
ATOM	1860	O	THR	449	32.068	32.953	6.006	1.00	28.97
ATOM	1861	N	THR	450	33.380	34.628	5.256	1.00	27.76
ATOM	1862	CA	THR	450	32.668	35.638	6.008	1.00	26.60
ATOM	1863	CB	THR	450	33.600	36.759	6.469	1.00	27.00
ATOM	1864	OG1	THR	450	34.613	36.202	7.324	1.00	26.73
ATOM	1865	CG2	THR	450	32.812	37.819	7.247	1.00	25.31
ATOM	1866	C	THR	450	31.578	36.145	5.076	1.00	26.94
ATOM	1867	O	THR	450	31.856	36.685	4.003	1.00	26.91
ATOM	1868	N	LEU	451	30.333	35.896	5.464	1.00	26.50
ATOM	1869	CA	LEU	451	29.184	36.267	4.661	1.00	25.37
ATOM	1870	CB	LEU	451	28.401	35.007	4.294	1.00	25.61
ATOM	1871	CG	LEU	451	29.076	33.801	3.662	1.00	26.81
ATOM	1872	CD1	LEU	451	28.101	32.649	3.739	1.00	27.81
ATOM	1873	CD2	LEU	451	29.459	34.096	2.220	1.00	26.32
ATOM	1874	C	LEU	451	28.215	37.168	5.399	1.00	24.26
ATOM	1875	O	LEU	451	28.287	37.313	6.622	1.00	23.50
ATOM	1876	N	PRO	452	27.324	37.834	4.646	1.00	22.96
ATOM	1877	CD	PRO	452	27.281	37.930	3.174	1.00	23.01
ATOM	1878	CA	PRO	452	26.328	38.707	5.252	1.00	21.34
ATOM	1879	CB	PRO	452	25.528	39.189	4.045	1.00	22.18
ATOM	1880	CG	PRO	452	26.545	39.213	2.957	1.00	23.73
ATOM	1881	C	PRO	452	25.490	37.742	6.069	1.00	20.41
ATOM	1882	O	PRO	452	25.315	36.587	5.674	1.00	20.81
ATOM	1883	N	GLN	453	24.983	38.197	7.201	1.00	19.57
ATOM	1884	CA	GLN	453	24.179	37.334	8.053	1.00	18.59
ATOM	1885	CB	GLN	453	23.888	38.047	9.364	1.00	18.03
ATOM	1886	CG	GLN	453	22.915	39.183	9.194	1.00	16.29
ATOM	1887	CD	GLN	453	22.857	40.088	10.384	1.00	17.25
ATOM	1888	OE1	GLN	453	22.521	41.259	10.244	1.00	18.98
ATOM	1889	NE2	GLN	453	23.184	39.565	11.571	1.00	12.28
ATOM	1890	C	GLN	453	22.861	37.023	7.368	1.00	19.31
ATOM	1891	O	GLN	453	22.451	37.735	6.445	1.00	19.70
ATOM	1892	N	ASP	454	22.215	35.939	7.786	1.00	19.47
ATOM	1893	CA	ASP	454	20.915	35.592	7.225	1.00	20.05
ATOM	1894	CB	ASP	454	20.831	34.095	6.866	1.00	20.04
ATOM	1895	CG	ASP	454	20.782	33.200	8.086	1.00	22.40
ATOM	1896	OD1	ASP	454	21.568	33.406	9.032	1.00	22.31
ATOM	1897	OD2	ASP	454	19.926	32.296	8.103	1.00	25.12
ATOM	1898	C	ASP	454	19.883	36.001	8.281	1.00	19.45
ATOM	1899	O	ASP	454	20.250	36.565	9.309	1.00	19.72
ATOM	1900	N	ALA	455	18.607	35.720	8.041	1.00	20.44
ATOM	1901	CA	ALA	455	17.544	36.083	8.986	1.00	20.48
ATOM	1902	CB	ALA	455	16.178	35.765	8.390	1.00	17.68
ATOM	1903	C	ALA	455	17.662	35.469	10.330	1.00	19.73
ATOM	1904	O	ALA	455	17.265	36.091	11.368	1.00	22.40
ATOM	1905	N	VAL	456	18.147	34.234	10.462	1.00	20.09
ATOM	1906	CA	VAL	456	18.295	33.564	11.754	1.00	19.00
ATOM	1907	CB	VAL	456	18.746	32.099	11.578	1.00	19.21
ATOM	1908	CG1	VAL	456	19.143	31.485	12.933	1.00	17.42
ATOM	1909	CG2	VAL	456	17.636	31.293	10.917	1.00	16.27

ATOM	1910	C	VAL	456	19.316	34.319	12.594	1.00	17.87
ATOM	1911	O	VAL	456	19.062	34.642	13.744	1.00	18.04
ATOM	1912	N	SER	457	20.438	34.660	11.972	1.00	19.53
ATOM	1913	CA	SER	457	21.517	35.392	12.630	1.00	19.10
ATOM	1914	CB	SER	457	22.673	35.589	11.644	1.00	17.70
ATOM	1915	OG	SER	457	23.631	36.508	12.143	1.00	20.26
ATOM	1916	C	SER	457	21.049	36.745	13.157	1.00	18.37
ATOM	1917	O	SER	457	21.246	37.063	14.324	1.00	18.88
ATOM	1918	N	ARG	458	20.402	37.519	12.292	1.00	18.67
ATOM	1919	CA	ARG	458	19.916	38.851	12.636	1.00	18.34
ATOM	1920	CB	ARG	458	19.356	39.551	11.389	1.00	15.93
ATOM	1921	CG	ARG	458	19.049	41.042	11.573	1.00	15.45
ATOM	1922	CD	ARG	458	18.892	41.721	10.220	1.00	13.63
ATOM	1923	NE	ARG	458	18.931	43.176	10.303	1.00	14.59
ATOM	1924	CZ	ARG	458	19.865	43.935	9.733	1.00	16.49
ATOM	1925	NH1	ARG	458	19.816	45.257	9.859	1.00	18.89
ATOM	1926	NH2	ARG	458	20.871	43.377	9.062	1.00	17.85
ATOM	1927	C	ARG	458	18.863	38.798	13.723	1.00	18.62
ATOM	1928	O	ARG	458	18.924	39.562	14.674	1.00	18.82
ATOM	1929	N	THR	459	17.900	37.896	13.580	1.00	20.47
ATOM	1930	CA	THR	459	16.831	37.759	14.571	1.00	22.62
ATOM	1931	CB	THR	459	15.759	36.708	14.120	1.00	23.54
ATOM	1932	OG1	THR	459	15.175	37.109	12.872	1.00	23.92
ATOM	1933	CG2	THR	459	14.655	36.566	15.168	1.00	23.27
ATOM	1934	C	THR	459	17.395	37.354	15.939	1.00	22.25
ATOM	1935	O	THR	459	16.988	37.896	16.974	1.00	22.42
ATOM	1936	N	GLN	460	18.324	36.400	15.945	1.00	21.83
ATOM	1937	CA	GLN	460	18.913	35.943	17.196	1.00	23.58
ATOM	1938	CB	GLN	460	19.575	34.574	17.022	1.00	28.20
ATOM	1939	CG	GLN	460	18.532	33.481	16.700	1.00	34.19
ATOM	1940	CD	GLN	460	19.106	32.076	16.567	1.00	38.92
ATOM	1941	OE1	GLN	460	18.389	31.140	16.174	1.00	41.47
ATOM	1942	NE2	GLN	460	20.386	31.910	16.903	1.00	41.20
ATOM	1943	C	GLN	460	19.847	36.972	17.814	1.00	21.76
ATOM	1944	O	GLN	460	19.841	37.167	19.024	1.00	22.18
ATOM	1945	N	ARG	461	20.601	37.677	16.983	1.00	20.55
ATOM	1946	CA	ARG	461	21.490	38.710	17.485	1.00	19.90
ATOM	1947	CB	ARG	461	22.460	39.178	16.398	1.00	18.96
ATOM	1948	CG	ARG	461	23.810	38.533	16.562	1.00	18.17
ATOM	1949	CD	ARG	461	24.341	37.840	15.337	1.00	20.30
ATOM	1950	NE	ARG	461	25.088	38.742	14.479	1.00	21.22
ATOM	1951	CZ	ARG	461	26.196	38.426	13.812	1.00	20.58
ATOM	1952	NH1	ARG	461	26.740	37.220	13.886	1.00	18.60
ATOM	1953	NH2	ARG	461	26.716	39.316	12.992	1.00	23.17
ATOM	1954	C	ARG	461	20.661	39.855	18.042	1.00	20.36
ATOM	1955	O	ARG	461	20.824	40.229	19.201	1.00	21.32
ATOM	1956	N	ARG	462	19.724	40.366	17.247	1.00	20.67
ATOM	1957	CA	ARG	462	18.847	41.453	17.685	1.00	20.84
ATOM	1958	CB	ARG	462	17.857	41.820	16.574	1.00	21.40
ATOM	1959	CG	ARG	462	16.931	42.969	16.941	1.00	22.08
ATOM	1960	CD	ARG	462	15.792	43.156	15.944	1.00	21.34
ATOM	1961	NE	ARG	462	14.330	42.052	16.007	1.00	21.80
ATOM	1962	CZ	ARG	462	13.742	41.978	15.247	1.00	21.21
ATOM	1963	NH1	ARG	462	12.935	40.937	15.371	1.00	22.57
ATOM	1964	NH2	ARG	462	13.459	42.929	14.367	1.00	18.74
ATOM	1965	C	ARG	462	18.056	41.013	18.926	1.00	21.55
ATOM	1966	O	ARG	462	17.801	41.822	19.933	1.00	21.69
ATOM	1967	N	GLY	463	17.711	39.731	18.965	1.00	21.06

ATOM	1968	CA	GLY	463	16.950	39.173	20.064	1.00	21.40
ATOM	1969	C	GLY	463	17.594	39.194	21.434	1.00	23.27
ATOM	1970	O	GLY	463	16.951	38.847	22.420	1.00	25.42
ATOM	1971	N	ARG	464	18.856	39.586	21.522	1.00	24.33
ATOM	1972	CA	ARG	464	19.530	39.644	22.814	1.00	25.08
ATOM	1973	CB	ARG	464	21.044	39.714	22.620	1.00	25.94
ATOM	1974	CG	ARG	464	21.632	38.564	21.823	1.00	28.27
ATOM	1975	CD	ARG	464	21.511	37.237	22.554	1.00	31.16
ATOM	1976	NE	ARG	464	22.670	36.393	22.274	1.00	35.52
ATOM	1977	CZ	ARG	464	22.887	35.766	21.119	1.00	39.25
ATOM	1978	NH1	ARG	464	23.987	35.031	20.963	1.00	40.53
ATOM	1979	NH2	ARG	464	21.991	35.828	20.132	1.00	39.41
ATOM	1980	C	ARG	464	19.042	40.848	23.634	1.00	25.24
ATOM	1981	O	ARG	464	19.297	40.933	24.843	1.00	24.97
ATOM	1982	N	THR	465	18.360	41.784	22.975	1.00	25.46
ATOM	1983	CA	THR	465	17.821	42.970	23.651	1.00	25.46
ATOM	1984	CB	THR	465	18.428	44.286	23.081	1.00	22.61
ATOM	1985	OG1	THR	465	18.181	45.357	23.993	1.00	21.95
ATOM	1986	CG2	THR	465	17.831	44.644	21.731	1.00	19.47
ATOM	1987	C	THR	465	16.285	42.987	23.545	1.00	27.08
ATOM	1988	O	THR	465	15.697	42.133	22.874	1.00	27.65
ATOM	1989	N	GLY	466	15.644	43.931	24.230	1.00	28.70
ATOM	1990	CA	GLY	466	14.194	44.025	24.192	1.00	30.14
ATOM	1991	C	GLY	466	13.486	42.861	24.871	1.00	31.44
ATOM	1992	O	GLY	466	12.354	42.508	24.512	1.00	32.18
ATOM	1993	N	ARG	467	14.135	42.280	25.875	1.00	32.23
ATOM	1994	CA	ARG	467	13.578	41.143	26.600	1.00	32.05
ATOM	1995	CB	ARG	467	14.679	40.144	26.937	1.00	29.85
ATOM	1996	CG	ARG	467	15.369	39.574	25.734	1.00	28.91
ATOM	1997	CD	ARG	467	16.432	38.620	26.174	1.00	30.63
ATOM	1998	NE	ARG	467	17.122	38.018	25.044	1.00	33.36
ATOM	1999	CZ	ARG	467	17.549	36.760	25.027	1.00	35.37
ATOM	2000	NH1	ARG	467	18.173	36.275	23.959	1.00	36.51
ATOM	2001	NH2	ARG	467	17.370	35.987	26.088	1.00	36.08
ATOM	2002	C	ARG	467	12.858	41.567	27.873	1.00	33.30
ATOM	2003	O	ARG	467	13.431	41.573	28.963	1.00	34.17
ATOM	2004	N	GLY	468	11.583	41.898	27.732	1.00	34.55
ATOM	2005	CA	GLY	468	10.808	42.314	28.882	1.00	34.38
ATOM	2006	C	GLY	468	10.967	43.791	29.163	1.00	34.53
ATOM	2007	O	GLY	468	10.558	44.274	30.213	1.00	36.37
ATOM	2008	N	LYS	469	11.590	44.503	28.237	1.00	33.19
ATOM	2009	CA	LYS	469	11.787	45.932	28.379	1.00	32.67
ATOM	2010	CB	LYS	469	12.797	46.258	29.491	1.00	34.53
ATOM	2011	CG	LYS	469	14.257	45.905	29.206	1.00	35.53
ATOM	2012	CD	LYS	469	15.157	46.408	30.336	1.00	35.50
ATOM	2013	CE	LYS	469	16.634	46.384	29.961	1.00	36.18
ATOM	2014	NZ	LYS	469	17.508	46.793	31.105	1.00	33.86
ATOM	2015	C	LYS	469	12.291	46.417	27.045	1.00	31.65
ATOM	2016	O	LYS	469	12.765	45.627	26.234	1.00	32.31
ATOM	2017	N	PRO	470	12.154	47.717	26.778	1.00	30.75
ATOM	2018	CD	PRO	470	11.491	48.754	27.530	1.00	30.88
ATOM	2019	CA	PRO	470	12.626	48.255	25.500	1.00	28.89
ATOM	2020	CB	PRO	470	12.238	49.731	25.597	1.00	29.64
ATOM	2021	CG	PRO	470	11.044	49.721	26.519	1.00	30.22
ATOM	2022	C	PRO	470	14.130	48.089	25.298	1.00	27.83
ATOM	2023	O	PRO	470	14.910	48.069	26.256	1.00	28.39
ATOM	2024	N	GLY	471	14.525	47.975	24.040	1.00	25.46
ATOM	2025	CA	GLY	471	15.923	47.834	23.701	1.00	22.38

ATOM	2026	C	GLY	471	16.164	48.513	22.373	1.00	20.97
ATOM	2027	O	GLY	471	15.216	48.887	21.668	1.00	20.48
ATOM	2028	N	ILE	472	17.431	48.715	22.043	1.00	20.35
ATOM	2029	CA	ILE	472	17.803	49.344	20.792	1.00	19.19
ATOM	2030	CB	ILE	472	18.500	50.710	21.018	1.00	19.31
ATOM	2031	CG2	ILE	472	18.916	51.317	19.697	1.00	19.60
ATOM	2032	CG1	ILE	472	17.534	51.680	21.706	1.00	20.42
ATOM	2033	CD1	ILE	472	18.101	53.048	21.989	1.00	20.47
ATOM	2034	C	ILE	472	18.727	48.400	20.045	1.00	20.13
ATOM	2035	O	ILE	472	19.509	47.650	20.651	1.00	18.96
ATOM	2036	N	TYR	473	18.593	48.402	18.726	1.00	20.53
ATOM	2037	CA	TYR	473	19.406	47.562	17.865	1.00	20.24
ATOM	2038	CB	TYR	473	18.527	46.504	17.184	1.00	17.07
ATOM	2039	CG	TYR	473	19.236	45.657	16.154	1.00	16.23
ATOM	2040	CD1	TYR	473	20.183	44.704	16.537	1.00	16.38
ATOM	2041	CE1	TYR	473	20.844	43.918	15.594	1.00	15.97
ATOM	2042	CD2	TYR	473	18.961	45.809	14.792	1.00	15.90
ATOM	2043	CE2	TYR	473	19.615	45.033	13.830	1.00	17.92
ATOM	2044	CZ	TYR	473	20.561	44.085	14.236	1.00	19.05
ATOM	2045	OH	TYR	473	21.232	43.322	13.292	1.00	16.03
ATOM	2046	C	TYR	473	20.054	48.481	16.839	1.00	20.38
ATOM	2047	O	TYR	473	19.372	49.235	16.156	1.00	21.81
ATOM	2048	N	ARG	474	21.377	48.486	16.795	1.00	21.07
ATOM	2049	CA	ARG	474	22.087	49.311	15.833	1.00	21.12
ATOM	2050	CB	ARG	474	23.092	50.217	16.535	1.00	22.36
ATOM	2051	CG	ARG	474	22.454	51.054	17.627	1.00	24.18
ATOM	2052	CD	ARG	474	23.444	51.980	18.304	1.00	25.34
ATOM	2053	NE	ARG	474	22.844	52.571	19.493	1.00	26.57
ATOM	2054	CZ	ARG	474	21.960	53.562	19.476	1.00	26.60
ATOM	2055	NH1	ARG	474	21.468	54.026	20.615	1.00	25.83
ATOM	2056	NH2	ARG	474	21.580	54.105	18.327	1.00	27.33
ATOM	2057	C	ARG	474	22.766	48.354	14.876	1.00	21.22
ATOM	2058	O	ARG	474	23.282	47.310	15.281	1.00	21.04
ATOM	2059	N	PHE	475	22.740	48.699	13.599	1.00	22.21
ATOM	2060	CA	PHE	475	23.306	47.849	12.575	1.00	23.28
ATOM	2061	CB	PHE	475	22.170	47.148	11.815	1.00	25.19
ATOM	2062	CG	PHE	475	21.164	48.103	11.199	1.00	26.26
ATOM	2063	CD1	PHE	475	20.079	48.570	11.941	1.00	25.75
ATOM	2064	CD2	PHE	475	21.307	48.537	9.878	1.00	26.21
ATOM	2065	CE1	PHE	475	19.156	49.452	11.374	1.00	24.75
ATOM	2066	CE2	PHE	475	20.390	49.417	9.306	1.00	24.17
ATOM	2067	CZ	PHE	475	19.314	49.873	10.060	1.00	23.51
ATOM	2068	C	PHE	475	24.151	48.638	11.598	1.00	23.82
ATOM	2069	O	PHE	475	23.960	49.843	11.428	1.00	25.90
ATOM	2070	N	VAL	476	25.082	47.946	10.955	1.00	23.60
ATOM	2071	CA	VAL	476	25.957	48.545	9.959	1.00	22.75
ATOM	2072	CB	VAL	476	27.299	47.772	9.898	1.00	23.15
ATOM	2073	CG1	VAL	476	28.178	48.292	8.773	1.00	22.36
ATOM	2074	CG2	VAL	476	28.019	47.881	11.227	1.00	23.76
ATOM	2075	C	VAL	476	25.253	48.440	8.594	1.00	21.91
ATOM	2076	O	VAL	476	25.323	49.353	7.774	1.00	22.30
ATOM	2077	N	ALA	477	24.590	47.320	8.371	1.00	21.29
ATOM	2078	CA	ALA	477	23.919	47.066	7.111	1.00	21.64
ATOM	2079	CB	ALA	477	24.658	45.974	6.328	1.00	21.33
ATOM	2080	C	ALA	477	22.454	46.696	7.301	1.00	21.13
ATOM	2081	O	ALA	477	22.091	45.952	8.218	1.00	20.40
ATOM	2082	N	PRO	478	21.598	47.195	6.403	1.00	21.02
ATOM	2083	CD	PRO	478	21.990	48.162	5.360	1.00	21.21

ATOM	2084	CA	PRO	478	20.152	46.976	6.400	1.00	23.06
ATOM	2085	CB	PRO	478	19.648	48.180	5.601	1.00	23.71
ATOM	2086	CG	PRO	478	20.722	48.326	4.561	1.00	23.74
ATOM	2087	C	PRO	478	19.669	45.653	5.791	1.00	21.67
ATOM	2088	O	PRO	478	18.532	45.226	6.028	1.00	21.26
ATOM	2089	N	GLY	479	20.515	45.021	4.992	1.00	19.99
ATOM	2090	CA	GLY	479	20.118	43.779	4.368	1.00	19.25
ATOM	2091	C	GLY	479	20.473	42.550	5.166	1.00	19.67
ATOM	2092	O	GLY	479	21.255	42.611	6.117	1.00	19.75
ATOM	2093	N	GLU	480	19.892	41.430	4.762	1.00	18.74
ATOM	2094	CA	GLU	480	20.135	40.145	5.395	1.00	19.62
ATOM	2095	CB	GLU	480	19.266	39.994	6.641	1.00	19.51
ATOM	2096	CG	GLU	480	17.798	39.867	6.293	1.00	20.84
ATOM	2097	CD	GLU	480	16.907	39.754	7.487	1.00	20.69
ATOM	2098	OE1	GLU	480	15.720	40.123	7.353	1.00	21.54
ATOM	2099	OE2	GLU	480	17.383	39.300	8.547	1.00	20.24
ATOM	2100	C	GLU	480	19.713	39.095	4.373	1.00	20.25
ATOM	2101	O	GLU	480	18.875	39.368	3.508	1.00	21.34
ATOM	2102	N	ARG	481	20.297	37.908	4.442	1.00	19.33
ATOM	2103	CA	ARG	481	19.916	36.858	3.515	1.00	18.50
ATOM	2104	CB	ARG	481	21.063	35.868	3.302	1.00	18.20
ATOM	2105	CG	ARG	481	22.241	36.404	2.523	1.00	15.86
ATOM	2106	CD	ARG	481	23.287	35.325	2.421	1.00	15.43
ATOM	2107	NE	ARG	481	23.964	35.096	3.694	1.00	14.91
ATOM	2108	CZ	ARG	481	23.950	33.946	4.367	1.00	15.54
ATOM	2109	NH1	ARG	481	23.279	32.903	3.897	1.00	15.94
ATOM	2110	NH2	ARG	481	24.642	33.826	5.495	1.00	11.48
ATOM	2111	C	ARG	481	18.744	36.118	4.118	1.00	19.75
ATOM	2112	O	ARG	481	18.698	35.898	5.332	1.00	19.19
ATOM	2113	N	PRO	482	17.726	35.814	3.303	1.00	21.15
ATOM	2114	CD	PRO	482	17.480	36.254	1.914	1.00	21.49
ATOM	2115	CA	PRO	482	16.577	35.081	3.848	1.00	21.68
ATOM	2116	CB	PRO	482	15.704	34.858	2.611	1.00	21.74
ATOM	2117	CG	PRO	482	15.976	36.100	1.785	1.00	22.13
ATOM	2118	C	PRO	482	17.096	33.749	4.422	1.00	21.37
ATOM	2119	O	PRO	482	18.049	33.166	3.896	1.00	21.05
ATOM	2120	N	SER	483	16.502	33.288	5.513	1.00	21.11
ATOM	2121	CA	SER	483	16.942	32.048	6.133	1.00	21.78
ATOM	2122	CB	SER	483	16.247	31.868	7.487	1.00	21.27
ATOM	2123	OG	SER	483	14.868	31.562	7.331	1.00	19.02
ATOM	2124	C	SER	483	16.591	30.860	5.251	1.00	22.57
ATOM	2125	O	SER	483	15.780	30.983	4.343	1.00	22.97
ATOM	2126	N	GLY	484	17.213	29.714	5.502	1.00	24.13
ATOM	2127	CA	GLY	484	16.835	28.539	4.747	1.00	26.14
ATOM	2128	C	GLY	484	17.833	27.793	3.904	1.00	27.18
ATOM	2129	O	GLY	484	17.500	26.727	3.387	1.00	28.70
ATOM	2130	N	MET	485	19.028	28.337	3.722	1.00	27.71
ATOM	2131	CA	MET	485	20.027	27.653	2.913	1.00	27.75
ATOM	2132	CB	MET	485	20.517	28.557	1.782	1.00	30.73
ATOM	2133	CG	MET	485	19.436	29.106	0.850	1.00	36.02
ATOM	2134	SD	MET	485	18.683	27.861	-0.207	1.00	42.25
ATOM	2135	CE	MET	485	20.139	26.751	-0.591	1.00	41.08
ATOM	2136	C	MET	485	21.221	27.259	3.759	1.00	25.31
ATOM	2137	O	MET	485	21.559	27.941	4.726	1.00	23.50
ATOM	2138	N	PHE	486	21.812	26.116	3.443	1.00	25.36
ATOM	2139	CA	PHE	486	23.018	25.693	4.138	1.00	25.36
ATOM	2140	CB	PHE	486	22.745	24.797	5.359	1.00	23.40
ATOM	2141	CG	PHE	486	22.193	23.445	5.035	1.00	24.70

ATOM	2142	CD1	PHE	486	23.048	22.371	4.795	1.00	25.53
ATOM	2143	CD2	PHE	486	20.822	23.226	5.034	1.00	23.72
ATOM	2144	CE1	PHE	486	22.549	21.098	4.564	1.00	25.73
ATOM	2145	CE2	PHE	486	20.311	21.959	4.804	1.00	25.05
ATOM	2146	CZ	PHE	486	21.174	20.887	4.569	1.00	25.77
ATOM	2147	C	PHE	486	24.004	25.089	3.141	1.00	24.60
ATOM	2148	O	PHE	486	23.616	24.599	2.075	1.00	22.55
ATOM	2149	N	ASP	487	25.282	25.232	3.465	1.00	25.33
ATOM	2150	CA	ASP	487	26.392	24.769	2.639	1.00	25.56
ATOM	2151	CB	ASP	487	27.674	25.435	3.150	1.00	25.82
ATOM	2152	CG	ASP	487	28.810	25.337	2.174	1.00	25.43
ATOM	2153	OD1	ASP	487	28.767	26.041	1.155	1.00	26.83
ATOM	2154	OD2	ASP	487	29.752	24.568	2.421	1.00	26.93
ATOM	2155	C	ASP	487	26.590	23.244	2.582	1.00	26.12
ATOM	2156	O	ASP	487	26.323	22.518	3.548	1.00	26.16
ATOM	2157	N	SER	488	27.134	22.781	1.462	1.00	26.57
ATOM	2158	CA	SER	488	27.421	21.365	1.244	1.00	26.60
ATOM	2159	CB	SER	488	27.972	21.165	-0.173	1.00	28.61
ATOM	2160	OG	SER	488	28.173	19.795	-0.481	1.00	31.93
ATOM	2161	C	SER	488	28.421	20.838	2.286	1.00	26.05
ATOM	2162	O	SER	488	28.447	19.639	2.583	1.00	26.13
ATOM	2163	N	SER	489	29.227	21.728	2.861	1.00	24.66
ATOM	2164	CA	SER	489	30.185	21.301	3.864	1.00	22.91
ATOM	2165	CB	SER	489	31.078	22.459	4.300	1.00	21.25
ATOM	2166	OG	SER	489	30.310	23.551	4.768	1.00	21.37
ATOM	2167	C	SER	489	29.422	20.737	5.062	1.00	23.17
ATOM	2168	O	SER	489	29.978	19.963	5.846	1.00	24.42
ATOM	2169	N	VAL	490	28.156	21.129	5.216	1.00	21.89
ATOM	2170	CA	VAL	490	27.363	20.620	6.324	1.00	21.05
ATOM	2171	CB	VAL	490	26.038	21.396	6.522	1.00	21.77
ATOM	2172	CG1	VAL	490	25.220	20.725	7.598	1.00	20.51
ATOM	2173	CG2	VAL	490	26.314	22.853	6.931	1.00	20.48
ATOM	2174	C	VAL	490	27.088	19.147	6.051	1.00	20.91
ATOM	2175	O	VAL	490	27.114	18.341	6.973	1.00	22.47
ATOM	2176	N	LEU	491	26.879	18.793	4.779	1.00	21.01
ATOM	2177	CA	LEU	491	26.636	17.397	4.390	1.00	21.10
ATOM	2178	CB	LEU	491	26.283	17.289	2.909	1.00	20.22
ATOM	2179	CG	LEU	491	25.006	18.026	2.505	1.00	22.49
ATOM	2180	CD1	LEU	491	24.743	17.853	1.014	1.00	20.45
ATOM	2181	CD2	LEU	491	23.829	17.495	3.329	1.00	21.46
ATOM	2182	C	LEU	491	27.900	16.594	4.686	1.00	20.78
ATOM	2183	O	LEU	491	27.843	15.522	5.292	1.00	22.36
ATOM	2184	N	CYS	492	29.046	17.138	4.291	1.00	19.79
ATOM	2185	CA	CYS	492	30.317	16.491	4.556	1.00	19.65
ATOM	2186	CB	CYS	492	31.468	17.390	4.092	1.00	18.82
ATOM	2187	SG	CYS	492	33.106	16.704	4.401	1.00	20.38
ATOM	2188	C	CYS	492	30.413	16.274	6.067	1.00	19.87
ATOM	2189	O	CYS	492	30.801	15.205	6.537	1.00	20.08
ATOM	2190	N	GLU	493	29.997	17.289	6.817	1.00	21.33
ATOM	2191	CA	GLU	493	30.028	17.262	8.274	1.00	22.71
ATOM	2192	CB	GLU	493	29.724	18.648	8.830	1.00	24.31
ATOM	2193	CG	GLU	493	30.165	18.820	10.269	1.00	28.02
ATOM	2194	CD	GLU	493	30.042	20.247	10.763	1.00	29.49
ATOM	2195	OE1	GLU	493	29.269	21.030	10.166	1.00	31.62
ATOM	2196	OE2	GLU	493	30.720	20.585	11.758	1.00	32.33
ATOM	2197	C	GLU	493	29.074	16.229	8.862	1.00	21.21
ATOM	2198	O	GLU	493	29.344	15.663	9.925	1.00	21.52
ATOM	2199	N	CYS	494	27.975	15.969	8.161	1.00	20.48

ATOM	2200	CA	CYS	494	27.008	14.970	8.611	1.00	20.92
ATOM	2201	CB	CYS	494	25.690	15.097	7.830	1.00	20.47
ATOM	2202	SG	CYS	494	24.630	16.512	8.329	1.00	19.52
ATOM	2203	C	CYS	494	27.616	13.565	8.471	1.00	20.64
ATOM	2204	O	CYS	494	27.548	12.750	9.404	1.00	21.39
ATOM	2205	N	TYR	495	28.240	13.296	7.324	1.00	18.97
ATOM	2206	CA	TYR	495	28.886	12.008	7.092	1.00	20.35
ATOM	2207	CB	TYR	495	29.372	11.918	5.645	1.00	19.37
ATOM	2208	CG	TYR	495	28.260	11.676	4.653	1.00	19.50
ATOM	2209	CD1	TYR	495	27.606	12.740	4.038	1.00	19.12
ATOM	2210	CE1	TYR	495	26.557	12.524	3.146	1.00	18.63
ATOM	2211	CD2	TYR	495	27.840	10.378	4.348	1.00	18.29
ATOM	2212	CE2	TYR	495	26.794	10.154	3.461	1.00	18.31
ATOM	2213	CZ	TYR	495	26.158	11.229	2.866	1.00	18.52
ATOM	2214	OH	TYR	495	25.114	11.014	1.997	1.00	22.20
ATOM	2215	C	TYR	495	30.060	11.804	8.059	1.00	20.52
ATOM	2216	O	TYR	495	30.287	10.708	8.572	1.00	20.61
ATOM	2217	N	ASP	496	30.804	12.874	8.302	1.00	21.88
ATOM	2218	CA	ASP	496	31.934	12.834	9.212	1.00	23.32
ATOM	2219	CB	ASP	496	32.631	14.204	9.212	1.00	25.74
ATOM	2220	CG	ASP	496	33.981	14.190	9.928	1.00	28.22
ATOM	2221	OD1	ASP	496	35.028	14.310	9.252	1.00	27.49
ATOM	2222	OD2	ASP	496	33.995	14.083	11.172	1.00	29.66
ATOM	2223	C	ASP	496	31.433	12.459	10.613	1.00	24.14
ATOM	2224	O	ASP	496	32.051	11.639	11.302	1.00	24.65
ATOM	2225	N	ALA	497	30.291	13.023	11.007	1.00	25.27
ATOM	2226	CA	ALA	497	29.685	12.758	12.322	1.00	25.04
ATOM	2227	CB	ALA	497	28.555	13.746	12.592	1.00	26.49
ATOM	2228	C	ALA	497	29.169	11.327	12.464	1.00	25.23
ATOM	2229	O	ALA	497	29.274	10.718	13.540	1.00	24.69
ATOM	2230	N	GLY	498	28.571	10.807	11.397	1.00	24.53
ATOM	2231	CA	GLY	498	28.077	9.443	11.433	1.00	25.39
ATOM	2232	C	GLY	498	29.231	8.490	11.695	1.00	25.40
ATOM	2233	O	GLY	498	29.164	7.619	12.567	1.00	24.85
ATOM	2234	N	CME	499	30.314	8.708	10.960	1.00	25.32
ATOM	2235	CA	CME	499	31.527	7.908	11.068	1.00	25.32
ATOM	2236	C	CME	499	32.278	8.088	12.377	1.00	23.75
ATOM	2237	O	CME	499	32.746	7.116	12.958	1.00	23.80
ATOM	2238	CB	CME	499	32.475	8.244	9.917	1.00	25.58
ATOM	2239	SG	CME	499	31.828	7.806	8.284	1.00	25.23
ATOM	2240	2SG	CME	499	31.898	5.788	8.347	1.00	25.26
ATOM	2241	2CB	CME	499	33.623	5.432	7.900	1.00	22.20
ATOM	2242	2CA	CME	499	33.954	5.815	6.487	1.00	20.21
ATOM	2243	OG	CME	499	33.382	4.900	5.576	1.00	20.89
ATOM	2244	N	ALA	500	32.397	9.329	12.835	1.00	23.46
ATOM	2245	CA	ALA	500	33.126	9.619	14.068	1.00	23.38
ATOM	2246	CB	ALA	500	33.626	11.066	14.060	1.00	22.52
ATOM	2247	C	ALA	500	32.359	9.351	15.349	1.00	25.43
ATOM	2248	O	ALA	500	32.889	8.739	16.279	1.00	25.36
ATOM	2249	N	TRP	501	31.102	9.781	15.392	1.00	27.22
ATOM	2250	CA	TRP	501	30.303	9.623	16.601	1.00	28.60
ATOM	2251	CB	TRP	501	29.788	10.983	17.057	1.00	27.51
ATOM	2252	CG	TRP	501	30.851	11.978	17.305	1.00	25.74
ATOM	2253	CD2	TRP	501	31.598	12.149	18.510	1.00	23.93
ATOM	2254	CE2	TRP	501	32.450	13.254	18.319	1.00	24.45
ATOM	2255	CE3	TRP	501	31.631	11.477	19.732	1.00	23.70
ATOM	2256	CD1	TRP	501	31.270	12.947	16.450	1.00	25.45
ATOM	2257	NE1	TRP	501	32.230	13.725	17.052	1.00	26.50

ATOM	2258	CZ2	TRP	501	33.319	13.706	19.304	1.00	24.88
ATOM	2259	CZ3	TRP	501	32.498	11.924	20.712	1.00	24.31
ATOM	2260	CH2	TRP	501	33.331	13.028	20.493	1.00	25.27
ATOM	2261	C	TRP	501	29.116	8.675	16.639	1.00	29.45
ATOM	2262	O	TRP	501	28.799	8.155	17.708	1.00	31.24
ATOM	2263	N	TYR	502	28.452	8.442	15.512	1.00	29.45
ATOM	2264	CA	TYR	502	27.244	7.623	15.556	1.00	28.83
ATOM	2265	CB	TYR	502	26.064	8.418	14.987	1.00	26.77
ATOM	2266	CG	TYR	502	25.962	9.775	15.638	1.00	26.30
ATOM	2267	CD1	TYR	502	26.177	10.940	14.907	1.00	25.61
ATOM	2268	CE1	TYR	502	26.215	12.178	15.534	1.00	26.43
ATOM	2269	CD2	TYR	502	25.768	9.888	17.019	1.00	25.72
ATOM	2270	CE2	TYR	502	25.804	11.118	17.655	1.00	26.34
ATOM	2271	CZ	TYR	502	26.031	12.258	16.908	1.00	26.72
ATOM	2272	OH	TYR	502	26.103	13.475	17.541	1.00	29.21
ATOM	2273	C	TYR	502	27.268	6.226	15.004	1.00	29.90
ATOM	2274	O	TYR	502	26.218	5.623	14.808	1.00	30.51
ATOM	2275	N	GLU	503	28.459	5.688	14.795	1.00	30.61
ATOM	2276	CA	GLU	503	28.585	4.337	14.272	1.00	31.76
ATOM	2277	CB	GLU	503	28.115	3.320	15.300	1.00	33.16
ATOM	2278	CG	GLU	503	28.959	3.248	16.531	1.00	37.65
ATOM	2279	CD	GLU	503	28.810	1.913	17.218	1.00	42.70
ATOM	2280	OE1	GLU	503	27.654	1.459	17.415	1.00	44.39
ATOM	2281	OE2	GLU	503	29.854	1.304	17.541	1.00	46.49
ATOM	2282	C	GLU	503	27.781	4.150	13.008	1.00	30.99
ATOM	2283	O	GLU	503	27.274	3.062	12.740	1.00	32.02
ATOM	2284	N	LEU	504	27.670	5.212	12.224	1.00	31.39
ATOM	2285	CA	LEU	504	26.905	5.147	10.992	1.00	29.95
ATOM	2286	CB	LEU	504	25.963	6.351	10.864	1.00	26.33
ATOM	2287	CG	LEU	504	24.920	6.570	11.959	1.00	24.35
ATOM	2288	CD1	LEU	504	24.128	7.804	11.624	1.00	24.54
ATOM	2289	CD2	LEU	504	24.006	5.375	12.084	1.00	22.44
ATOM	2290	C	LEU	504	27.752	5.034	9.736	1.00	31.09
ATOM	2291	O	LEU	504	28.750	5.747	9.556	1.00	32.06
ATOM	2292	N	THR	505	27.323	4.116	8.883	1.00	29.82
ATOM	2293	CA	THR	505	27.918	3.847	7.590	1.00	28.87
ATOM	2294	CB	THR	505	27.336	2.520	7.067	1.00	29.51
ATOM	2295	OG1	THR	505	27.897	1.429	7.806	1.00	32.11
ATOM	2296	CG2	THR	505	27.595	2.337	5.612	1.00	31.82
ATOM	2297	C	THR	505	27.475	4.989	6.672	1.00	27.43
ATOM	2298	O	THR	505	26.390	5.542	6.857	1.00	28.06
ATOM	2299	N	PRO	506	28.302	5.367	5.680	1.00	26.19
ATOM	2300	CD	PRO	506	29.680	4.930	5.378	1.00	25.34
ATOM	2301	CA	PRO	506	27.895	6.456	4.784	1.00	24.28
ATOM	2302	CB	PRO	506	29.007	6.460	3.734	1.00	24.62
ATOM	2303	CG	PRO	506	30.212	6.083	4.533	1.00	23.11
ATOM	2304	C	PRO	506	26.529	6.153	4.165	1.00	24.09
ATOM	2305	O	PRO	506	25.705	7.046	3.990	1.00	22.93
ATOM	2306	N	ALA	507	26.291	4.880	3.855	1.00	24.47
ATOM	2307	CA	ALA	507	25.018	4.449	3.283	1.00	23.40
ATOM	2308	CB	ALA	507	25.079	2.968	2.912	1.00	22.33
ATOM	2309	C	ALA	507	23.871	4.715	4.269	1.00	23.01
ATOM	2310	O	ALA	507	22.786	5.133	3.866	1.00	22.45
ATOM	2311	N	GLU	508	24.123	4.488	5.555	1.00	22.85
ATOM	2312	CA	GLU	508	23.125	4.724	6.596	1.00	25.62
ATOM	2313	CB	GLU	508	23.593	4.149	7.936	1.00	26.13
ATOM	2314	CG	GLU	508	23.710	2.638	7.941	1.00	30.10
ATOM	2315	CD	GLU	508	24.322	2.069	9.217	1.00	32.11

ATOM	2316	OE1	GLU	508	24.722	2.840	10.110	1.00	34.14
ATOM	2317	OE2	GLU	508	24.406	0.828	9.323	1.00	35.16
ATOM	2318	C	GLU	508	22.849	6.222	6.743	1.00	26.03
ATOM	2319	O	GLU	508	21.694	6.635	6.843	1.00	26.78
ATOM	2320	N	THR	509	23.912	7.025	6.773	1.00	25.74
ATOM	2321	CA	THR	509	23.785	8.474	6.882	1.00	24.39
ATOM	2322	CB	THR	509	25.168	9.148	6.907	1.00	23.11
ATOM	2323	OG1	THR	509	25.853	8.790	8.113	1.00	20.57
ATOM	2324	CG2	THR	509	25.035	10.659	6.828	1.00	22.40
ATOM	2325	C	THR	509	22.973	9.000	5.692	1.00	25.46
ATOM	2326	O	THR	509	22.129	9.886	5.853	1.00	27.07
ATOM	2327	N	THR	510	23.193	8.421	4.513	1.00	24.22
ATOM	2328	CA	THR	510	22.471	8.825	3.314	1.00	23.80
ATOM	2329	CB	THR	510	22.992	8.074	2.087	1.00	23.34
ATOM	2330	OG1	THR	510	24.355	8.443	1.855	1.00	26.59
ATOM	2331	CG2	THR	510	22.193	8.429	0.870	1.00	22.93
ATOM	2332	C	THR	510	20.961	8.624	3.457	1.00	23.48
ATOM	2333	O	THR	510	20.174	9.456	3.013	1.00	23.82
ATOM	2334	N	VAL	511	20.565	7.529	4.098	1.00	24.04
ATOM	2335	CA	VAL	511	19.157	7.216	4.321	1.00	23.83
ATOM	2336	CB	VAL	511	19.019	5.872	5.072	1.00	25.13
ATOM	2337	CG1	VAL	511	17.577	5.644	5.509	1.00	24.67
ATOM	2338	CG2	VAL	511	19.480	4.729	4.168	1.00	24.94
ATOM	2339	C	VAL	511	18.482	8.329	5.122	1.00	22.86
ATOM	2340	O	VAL	511	17.391	8.783	4.783	1.00	23.35
ATOM	2341	N	ARG	512	19.160	8.779	6.168	1.00	22.63
ATOM	2342	CA	ARG	512	18.663	9.843	7.028	1.00	22.06
ATOM	2343	CB	ARG	512	19.465	9.846	8.325	1.00	20.58
ATOM	2344	CG	ARG	512	19.312	8.538	9.080	1.00	21.48
ATOM	2345	CD	ARG	512	20.435	8.307	10.076	1.00	22.08
ATOM	2346	NE	ARG	512	20.375	6.949	10.602	1.00	22.43
ATOM	2347	CZ	ARG	512	20.475	6.631	11.889	1.00	24.44
ATOM	2348	NH1	ARG	512	20.401	5.361	12.262	1.00	24.03
ATOM	2349	NH2	ARG	512	20.666	7.574	12.804	1.00	26.08
ATOM	2350	C	ARG	512	18.693	11.222	6.348	1.00	22.38
ATOM	2351	O	ARG	512	17.727	11.990	6.424	1.00	20.41
ATOM	2352	N	LEU	513	19.788	11.524	5.657	1.00	23.97
ATOM	2353	CA	LEU	513	19.907	12.802	4.970	1.00	23.82
ATOM	2354	CB	LEU	513	21.351	13.042	4.511	1.00	23.01
ATOM	2355	CG	LEU	513	22.412	13.142	5.619	1.00	22.43
ATOM	2356	CD1	LEU	513	23.758	13.482	5.030	1.00	20.55
ATOM	2357	CD2	LEU	513	22.027	14.191	6.637	1.00	21.42
ATOM	2358	C	LEU	513	18.923	12.860	3.800	1.00	23.93
ATOM	2359	O	LEU	513	18.388	13.917	3.481	1.00	26.02
ATOM	2360	N	ARG	514	18.641	11.714	3.196	1.00	23.65
ATOM	2361	CA	ARG	514	17.697	11.653	2.086	1.00	23.31
ATOM	2362	CB	ARG	514	17.726	10.259	1.461	1.00	24.64
ATOM	2363	CG	ARG	514	16.779	10.063	0.294	1.00	27.95
ATOM	2364	CD	ARG	514	17.055	11.033	-0.848	1.00	31.79
ATOM	2365	NE	ARG	514	18.388	10.876	-1.430	1.00	34.83
ATOM	2366	CZ	ARG	514	19.048	11.847	-2.057	1.00	35.11
ATOM	2367	NH1	ARG	514	20.251	11.608	-2.561	1.00	36.73
ATOM	2368	NH2	ARG	514	18.523	13.067	-2.154	1.00	34.93
ATOM	2369	C	ARG	514	16.289	11.997	1.595	1.00	23.18
ATOM	2370	O	ARG	514	15.598	12.822	2.010	1.00	23.43
ATOM	2371	N	ALA	515	15.892	11.396	3.714	1.00	22.98
ATOM	2372	CA	ALA	515	14.585	11.648	4.319	1.00	23.14
ATOM	2373	CB	ALA	515	14.434	10.936	5.537	1.00	22.55

ATOM	2374	C	ALA	515	14.430	13.135	4.630	1.00	23.92
ATOM	2375	O	ALA	515	13.382	13.721	4.379	1.00	23.30
ATOM	2376	N	TYR	516	15.483	13.734	5.181	1.00	24.72
ATOM	2377	CA	TYR	516	15.493	15.157	5.505	1.00	24.73
ATOM	2378	CB	TYR	516	16.860	15.537	6.077	1.00	20.83
ATOM	2379	CG	TYR	516	16.997	16.989	6.481	1.00	21.19
ATOM	2380	CD1	TYR	516	16.811	17.385	7.805	1.00	19.78
ATOM	2381	CE1	TYR	516	16.966	18.717	8.189	1.00	18.78
ATOM	2382	CD2	TYR	516	17.340	17.971	5.545	1.00	20.90
ATOM	2383	CE2	TYR	516	17.493	19.308	5.924	1.00	20.29
ATOM	2384	CZ	TYR	516	17.305	19.662	7.246	1.00	18.46
ATOM	2385	OH	TYR	516	17.473	20.960	7.626	1.00	21.53
ATOM	2386	C	TYR	516	15.213	15.963	4.226	1.00	26.41
ATOM	2387	O	TYR	516	14.390	16.883	4.218	1.00	26.36
ATOM	2388	N	MET	517	15.893	15.594	3.146	1.00	27.82
ATOM	2389	CA	MET	517	15.736	16.268	1.868	1.00	29.62
ATOM	2390	CB	MET	517	16.897	15.910	0.929	1.00	32.52
ATOM	2391	CG	MET	517	18.257	16.449	1.415	1.00	36.99
ATOM	2392	SD	MET	517	19.641	16.357	0.240	1.00	42.11
ATOM	2393	CE	MET	517	19.692	18.060	-0.335	1.00	41.79
ATOM	2394	C	MET	517	14.394	15.971	1.215	1.00	30.17
ATOM	2395	O	MET	517	13.863	16.793	0.484	1.00	31.65
ATOM	2396	N	ASN	518	13.824	14.813	1.507	1.00	30.49
ATOM	2397	CA	ASN	518	12.543	14.455	0.926	1.00	31.49
ATOM	2398	CB	ASN	518	12.338	12.941	0.965	1.00	33.77
ATOM	2399	CG	ASN	518	12.983	12.236	-0.210	1.00	35.89
ATOM	2400	OD1	ASN	518	13.269	12.852	-1.245	1.00	36.28
ATOM	2401	ND2	ASN	518	13.204	10.929	-0.065	1.00	35.87
ATOM	2402	C	ASN	518	11.359	15.146	1.585	1.00	32.06
ATOM	2403	O	ASN	518	10.242	15.100	1.059	1.00	33.11
ATOM	2404	N	THR	519	11.568	15.770	2.740	1.00	31.41
ATOM	2405	CA	THR	519	10.453	16.441	3.389	1.00	29.95
ATOM	2406	CB	THR	519	10.353	16.087	4.881	1.00	30.80
ATOM	2407	OG1	THR	519	11.403	16.723	5.606	1.00	36.48
ATOM	2408	CG2	THR	519	10.477	14.588	5.069	1.00	32.01
ATOM	2409	C	THR	519	10.435	17.955	3.166	1.00	28.51
ATOM	2410	O	THR	519	11.380	18.678	3.509	1.00	27.20
ATOM	2411	N	PRO	520	9.361	18.447	2.528	1.00	27.84
ATOM	2412	CD	PRO	520	8.275	17.657	1.919	1.00	27.48
ATOM	2413	CA	PRO	520	9.185	19.869	2.236	1.00	25.32
ATOM	2414	CB	PRO	520	7.850	19.891	1.491	1.00	25.57
ATOM	2415	CG	PRO	520	7.812	18.568	0.806	1.00	25.28
ATOM	2416	C	PRO	520	9.117	20.740	3.482	1.00	24.11
ATOM	2417	O	PRO	520	8.695	20.294	4.544	1.00	24.19
ATOM	2418	N	GLY	521	9.553	21.985	3.341	1.00	23.43
ATOM	2419	CA	GLY	521	9.491	22.931	4.437	1.00	23.18
ATOM	2420	C	GLY	521	10.708	23.045	5.313	1.00	23.53
ATOM	2421	O	GLY	521	10.690	23.813	6.279	1.00	23.92
ATOM	2422	N	LEU	522	11.744	22.267	5.010	1.00	23.75
ATOM	2423	CA	LEU	522	12.985	22.293	5.783	1.00	21.75
ATOM	2424	CB	LEU	522	13.448	20.860	6.099	1.00	20.22
ATOM	2425	CG	LEU	522	12.696	20.053	7.166	1.00	19.37
ATOM	2426	CD1	LEU	522	13.320	18.681	7.255	1.00	18.45
ATOM	2427	CD2	LEU	522	12.754	20.739	8.521	1.00	17.70
ATOM	2428	C	LEU	522	14.076	23.051	5.029	1.00	19.66
ATOM	2429	O	LEU	522	13.898	23.393	3.867	1.00	19.67
ATOM	2430	N	PRO	523	15.157	23.439	5.725	1.00	18.95
ATOM	2431	CD	PRO	523	15.328	23.445	7.187	1.00	16.62

ATOM	2432	CA	PRO	523	16.255	24.159	5.073	1.00	20.39
ATOM	2433	CB	PRO	523	17.270	24.305	6.208	1.00	19.00
ATOM	2434	CG	PRO	523	16.387	24.512	7.380	1.00	19.06
ATOM	2435	C	PRO	523	16.814	23.317	3.912	1.00	22.86
ATOM	2436	O	PRO	523	16.822	22.083	3.981	1.00	23.38
ATOM	2437	N	VAL	524	17.302	23.973	2.862	1.00	25.30
ATOM	2438	CA	VAL	524	17.819	23.250	1.707	1.00	27.02
ATOM	2439	CB	VAL	524	16.986	23.556	0.438	1.00	27.40
ATOM	2440	CG1	VAL	524	15.537	23.193	0.671	1.00	26.10
ATOM	2441	CG2	VAL	524	17.098	25.016	0.066	1.00	29.26
ATOM	2442	C	VAL	524	19.302	23.426	1.391	1.00	27.30
ATOM	2443	O	VAL	524	19.912	24.461	1.674	1.00	27.05
ATOM	2444	N	CYS	525	19.866	22.377	0.809	1.00	28.81
ATOM	2445	CA	CYS	525	21.260	22.331	0.397	1.00	30.97
ATOM	2446	CB	CYS	525	22.095	21.541	1.401	1.00	32.28
ATOM	2447	SG	CYS	525	21.430	19.886	1.803	1.00	38.03
ATOM	2448	C	CYS	525	21.285	21.617	-0.948	1.00	31.93
ATOM	2449	O	CYS	525	20.280	21.019	-1.365	1.00	31.91
ATOM	2450	N	GLN	526	22.416	21.699	-1.639	1.00	32.52
ATOM	2451	CA	GLN	526	22.557	21.053	-2.932	1.00	33.47
ATOM	2452	CB	GLN	526	23.831	21.525	-3.622	1.00	36.06
ATOM	2453	CG	GLN	526	23.797	22.989	-4.028	1.00	39.05
ATOM	2454	CD	GLN	526	25.143	23.497	-4.519	1.00	43.09
ATOM	2455	OE1	GLN	526	26.181	22.863	-4.302	1.00	44.20
ATOM	2456	NE2	GLN	526	25.134	24.648	-5.181	1.00	45.25
ATOM	2457	C	GLN	526	22.588	19.553	-2.709	1.00	32.95
ATOM	2458	O	GLN	526	23.203	19.070	-1.757	1.00	33.73
ATOM	2459	N	ASP	527	21.915	18.816	-3.580	1.00	32.09
ATOM	2460	CA	ASP	527	21.857	17.372	-3.459	1.00	31.50
ATOM	2461	CB	ASP	527	20.800	16.819	-4.421	1.00	33.07
ATOM	2462	CG	ASP	527	20.444	15.364	-4.145	1.00	34.64
ATOM	2463	OD1	ASP	527	19.441	14.898	-4.729	1.00	37.28
ATOM	2464	OD2	ASP	527	21.152	14.684	-3.363	1.00	36.58
ATOM	2465	C	ASP	527	23.220	16.747	-3.740	1.00	30.96
ATOM	2466	O	ASP	527	23.507	16.370	-4.877	1.00	30.98
ATOM	2467	N	HIS	528	24.070	16.673	-2.716	1.00	29.78
ATOM	2468	CA	HIS	528	25.408	16.079	-2.856	1.00	28.64
ATOM	2469	CB	HIS	528	26.500	17.060	-2.445	1.00	26.18
ATOM	2470	CG	HIS	528	26.610	18.248	-3.333	1.00	23.97
ATOM	2471	CD2	HIS	528	25.951	18.579	-4.468	1.00	23.60
ATOM	2472	ND1	HIS	528	27.483	19.281	-3.077	1.00	23.80
ATOM	2473	CE1	HIS	528	27.357	20.202	-4.015	1.00	24.23
ATOM	2474	NE2	HIS	528	26.433	19.801	-4.870	1.00	25.47
ATOM	2475	C	HIS	528	25.556	14.840	-1.997	1.00	28.65
ATOM	2476	O	HIS	528	26.657	14.516	-1.557	1.00	28.39
ATOM	2477	N	LEU	529	24.453	14.137	-1.776	1.00	29.34
ATOM	2478	CA	LEU	529	24.478	12.947	-0.942	1.00	29.62
ATOM	2479	CB	LEU	529	23.047	12.479	-0.645	1.00	29.60
ATOM	2480	CG	LEU	529	22.188	13.506	0.109	1.00	27.75
ATOM	2481	CD1	LEU	529	20.849	12.898	0.483	1.00	26.93
ATOM	2482	CD2	LEU	529	22.917	13.973	1.356	1.00	24.19
ATOM	2483	C	LEU	529	25.326	11.827	-1.540	1.00	29.38
ATOM	2484	O	LEU	529	26.158	11.237	-0.947	1.00	28.82
ATOM	2485	N	ALA	530	25.140	11.564	-2.830	1.00	29.06
ATOM	2486	CA	ALA	530	25.904	10.519	-3.508	1.00	29.34
ATOM	2487	CB	ALA	530	25.415	10.343	-4.951	1.00	29.19
ATOM	2488	C	ALA	530	27.394	10.856	-3.489	1.00	28.63
ATOM	2489	O	ALA	530	28.236	9.991	-3.217	1.00	29.57

ATOM	2490	N	PHE	531	27.709	12.125	-3.731	1.00	26.99
ATOM	2491	CA	PHE	531	29.094	12.553	-3.735	1.00	25.83
ATOM	2492	CB	PHE	531	29.232	14.024	-4.124	1.00	25.62
ATOM	2493	CG	PHE	531	30.621	14.553	-3.938	1.00	26.14
ATOM	2494	CD1	PHE	531	31.652	14.139	-4.778	1.00	26.59
ATOM	2495	CD2	PHE	531	30.918	15.398	-2.883	1.00	25.50
ATOM	2496	CE1	PHE	531	32.962	14.556	-4.564	1.00	25.76
ATOM	2497	CE2	PHE	531	32.222	15.820	-2.659	1.00	27.06
ATOM	2498	CZ	PHE	531	33.249	15.396	-3.502	1.00	26.12
ATOM	2499	C	PHE	531	29.769	12.325	-2.395	1.00	24.62
ATOM	2500	O	PHE	531	30.763	11.617	-2.328	1.00	26.66
ATOM	2501	N	TRP	532	29.222	12.900	-1.327	1.00	22.70
ATOM	2502	CA	TRP	532	29.824	12.758	-0.002	1.00	21.65
ATOM	2503	CB	TRP	532	29.145	13.682	1.006	1.00	20.94
ATOM	2504	CG	TRP	532	29.451	15.121	0.742	1.00	20.29
ATOM	2505	CD2	TRP	532	30.739	15.758	0.824	1.00	21.51
ATOM	2506	CE2	TRP	532	30.557	17.112	0.462	1.00	21.80
ATOM	2507	CE3	TRP	532	32.027	15.315	1.162	1.00	20.31
ATOM	2508	CD1	TRP	532	28.573	16.082	0.351	1.00	20.68
ATOM	2509	NE1	TRP	532	29.228	17.281	0.180	1.00	21.58
ATOM	2510	CZ2	TRP	532	31.618	18.037	0.428	1.00	21.77
ATOM	2511	CZ3	TRP	532	33.080	16.230	1.130	1.00	22.10
ATOM	2512	CH2	TRP	532	32.866	17.579	0.763	1.00	21.20
ATOM	2513	C	TRP	532	29.865	11.328	0.496	1.00	21.68
ATOM	2514	O	TRP	532	30.800	10.925	1.206	1.00	20.01
ATOM	2515	N	GLU	533	28.848	10.561	0.122	1.00	22.69
ATOM	2516	CA	GLU	533	28.787	9.159	0.488	1.00	23.84
ATOM	2517	CB	GLU	533	27.455	8.553	0.058	1.00	26.03
ATOM	2518	CG	GLU	533	27.279	7.129	0.543	1.00	26.87
ATOM	2519	CD	GLU	533	26.055	6.468	-0.018	1.00	27.26
ATOM	2520	OE1	GLU	533	25.058	7.165	-0.302	1.00	26.87
ATOM	2521	OE2	GLU	533	26.103	5.238	-0.185	1.00	30.58
ATOM	2522	C	GLU	533	29.926	8.450	-0.245	1.00	23.94
ATOM	2523	O	GLU	533	30.584	7.569	0.319	1.00	24.95
ATOM	2524	N	GLY	534	30.149	8.832	-1.502	1.00	23.38
ATOM	2525	CA	GLY	534	31.227	8.236	-2.277	1.00	23.87
ATOM	2526	C	GLY	534	32.555	8.469	-1.569	1.00	23.44
ATOM	2527	O	GLY	534	33.263	7.517	-1.214	1.00	22.74
ATOM	2528	N	VAL	535	32.829	9.739	-1.269	1.00	22.38
ATOM	2529	CA	VAL	535	34.050	10.147	-0.584	1.00	22.30
ATOM	2530	CB	VAL	535	34.037	11.674	-0.254	1.00	21.82
ATOM	2531	CG1	VAL	535	35.184	12.033	0.702	1.00	17.86
ATOM	2532	CG2	VAL	535	34.124	12.491	-1.541	1.00	17.05
ATOM	2533	C	VAL	535	34.312	9.351	0.696	1.00	22.60
ATOM	2534	O	VAL	535	35.324	8.655	0.799	1.00	23.81
ATOM	2535	N	PHE	536	33.381	9.411	1.645	1.00	22.80
ATOM	2536	CA	PHE	536	33.548	8.710	2.916	1.00	21.82
ATOM	2537	CB	PHE	536	32.496	9.169	3.931	1.00	21.01
ATOM	2538	CG	PHE	536	32.793	10.514	4.529	1.00	18.99
ATOM	2539	CD1	PHE	536	32.371	11.677	3.901	1.00	15.68
ATOM	2540	CD2	PHE	536	33.555	10.616	5.687	1.00	16.90
ATOM	2541	CE1	PHE	536	32.708	12.921	4.410	1.00	16.35
ATOM	2542	CE2	PHE	536	33.893	11.861	6.204	1.00	17.77
ATOM	2543	CZ	PHE	536	33.469	13.019	5.561	1.00	14.57
ATOM	2544	C	PHE	536	33.598	7.192	2.817	1.00	23.73
ATOM	2545	O	PHE	536	34.253	6.535	3.632	1.00	22.08
ATOM	2546	N	THR	537	32.941	6.633	1.805	1.00	26.19
ATOM	2547	CA	THR	537	32.952	5.189	1.619	1.00	28.54

ATOM	2548	CB	THR	537	31.998	4.771	0.490	1.00	29.40
ATOM	2549	OG1	THR	537	30.649	5.019	0.905	1.00	31.40
ATOM	2550	CG2	THR	537	32.148	3.287	0.174	1.00	29.35
ATOM	2551	C	THR	537	34.380	4.686	1.342	1.00	29.80
ATOM	2552	O	THR	537	34.741	3.566	1.722	1.00	30.70
ATOM	2553	N	GLY	538	35.201	5.537	0.733	1.00	29.84
ATOM	2554	CA	GLY	538	36.567	5.151	0.437	1.00	28.99
ATOM	2555	C	GLY	538	37.549	5.377	1.573	1.00	28.25
ATOM	2556	O	GLY	538	38.678	4.892	1.523	1.00	28.81
ATOM	2557	N	LEU	539	37.132	6.094	2.606	1.00	27.46
ATOM	2558	CA	LEU	539	38.020	6.375	3.720	1.00	27.32
ATOM	2559	CB	LEU	539	37.655	7.707	4.378	1.00	26.09
ATOM	2560	CG	LEU	539	37.583	8.951	3.481	1.00	24.55
ATOM	2561	CD1	LEU	539	37.394	10.159	4.367	1.00	23.67
ATOM	2562	CD2	LEU	539	38.843	9.108	2.645	1.00	24.83
ATOM	2563	C	LEU	539	37.963	5.248	4.725	1.00	28.87
ATOM	2564	O	LEU	539	37.689	5.458	5.909	1.00	30.15
ATOM	2565	N	THR	540	38.259	4.047	4.250	1.00	29.75
ATOM	2566	CA	THR	540	38.224	2.872	5.098	1.00	30.28
ATOM	2567	CB	THR	540	37.875	1.625	4.277	1.00	30.11
ATOM	2568	OG1	THR	540	38.931	1.351	3.352	1.00	30.87
ATOM	2569	CG2	THR	540	36.591	1.858	3.492	1.00	31.21
ATOM	2570	C	THR	540	39.533	2.652	5.857	1.00	30.76
ATOM	2571	O	THR	540	40.573	3.203	5.509	1.00	30.52
ATOM	2572	N	HIS	541	39.452	1.859	6.921	1.00	31.78
ATOM	2573	CA	HIS	541	40.603	1.524	7.757	1.00	31.88
ATOM	2574	CB	HIS	541	41.605	0.652	6.969	1.00	31.23
ATOM	2575	C	HIS	541	41.295	2.741	8.365	1.00	30.69
ATOM	2576	O	HIS	541	42.461	2.992	8.097	1.00	33.64
ATOM	2577	N	ILE	542	40.581	3.483	9.202	1.00	29.88
ATOM	2578	CA	ILE	542	41.149	4.661	9.852	1.00	29.84
ATOM	2579	CB	ILE	542	40.032	5.650	10.323	1.00	28.82
ATOM	2580	CG2	ILE	542	39.306	5.107	11.560	1.00	27.39
ATOM	2581	CG1	ILE	542	40.622	7.021	10.661	1.00	26.39
ATOM	2582	CD1	ILE	542	39.573	8.090	10.915	1.00	22.88
ATOM	2583	C	ILE	542	41.912	4.172	11.068	1.00	31.23
ATOM	2584	O	ILE	542	41.687	3.052	11.523	1.00	32.59
ATOM	2585	N	ASP	543	42.833	4.978	11.583	1.00	32.70
ATOM	2586	CA	ASP	543	43.558	4.580	12.778	1.00	33.07
ATOM	2587	CB	ASP	543	44.882	5.326	12.906	1.00	32.63
ATOM	2588	CG	ASP	543	45.667	4.909	14.136	1.00	34.41
ATOM	2589	OD1	ASP	543	46.261	3.815	14.106	1.00	37.12
ATOM	2590	OD2	ASP	543	45.698	5.666	15.135	1.00	35.50
ATOM	2591	C	ASP	543	42.636	4.978	13.914	1.00	34.38
ATOM	2592	O	ASP	543	42.306	6.160	14.067	1.00	34.89
ATOM	2593	N	ALA	544	42.206	3.997	14.702	1.00	34.33
ATOM	2594	CA	ALA	544	41.307	4.260	15.820	1.00	34.13
ATOM	2595	CB	ALA	544	40.876	2.956	16.460	1.00	34.20
ATOM	2596	C	ALA	544	41.873	5.212	16.876	1.00	34.61
ATOM	2597	O	ALA	544	41.133	5.998	17.463	1.00	34.47
ATOM	2598	N	HIS	545	43.180	5.159	17.113	1.00	36.16
ATOM	2599	CA	HIS	545	43.782	6.035	18.111	1.00	36.63
ATOM	2600	CB	HIS	545	45.216	5.635	18.445	1.00	38.84
ATOM	2601	CG	HIS	545	45.902	6.604	19.362	1.00	41.47
ATOM	2602	CD2	HIS	545	47.105	7.221	19.272	1.00	41.30
ATOM	2603	ND1	HIS	545	45.320	7.068	20.523	1.00	42.23
ATOM	2604	CE1	HIS	545	46.136	7.927	21.110	1.00	42.36
ATOM	2605	NE2	HIS	545	47.225	8.039	20.371	1.00	42.08

ATOM	2606	C	HIS	545	43.773	7.491	17.709	1.00	36.37
ATOM	2607	O	HIS	545	43.606	8.358	18.561	1.00	37.33
ATOM	2608	N	PHE	546	44.043	7.767	16.437	1.00	35.97
ATOM	2609	CA	PHE	546	44.044	9.148	15.958	1.00	36.04
ATOM	2610	CB	PHE	546	44.565	9.232	14.520	1.00	35.63
ATOM	2611	CG	PHE	546	46.052	9.084	14.405	1.00	35.41
ATOM	2612	CD1	PHE	546	46.890	9.545	15.411	1.00	35.87
ATOM	2613	CD2	PHE	546	46.618	8.471	13.292	1.00	36.70
ATOM	2614	CE1	PHE	546	48.264	9.397	15.310	1.00	35.65
ATOM	2615	CE2	PHE	546	47.996	8.317	13.183	1.00	34.51
ATOM	2616	CZ	PHE	546	48.817	8.779	14.192	1.00	35.18
ATOM	2617	C	PHE	546	42.632	9.713	16.041	1.00	35.77
ATOM	2618	O	PHE	546	42.435	10.845	16.486	1.00	34.76
ATOM	2619	N	LEU	547	41.655	8.898	15.643	1.00	36.27
ATOM	2620	CA	LEU	547	40.244	9.287	15.673	1.00	36.99
ATOM	2621	CB	LEU	547	39.365	8.134	15.188	1.00	35.89
ATOM	2622	CG	LEU	547	37.856	8.399	15.168	1.00	35.86
ATOM	2623	CD1	LEU	547	37.535	9.650	14.342	1.00	34.64
ATOM	2624	CD2	LEU	547	37.143	7.178	14.609	1.00	35.41
ATOM	2625	C	LEU	547	39.824	9.718	17.075	1.00	37.45
ATOM	2626	O	LEU	547	39.218	10.776	17.253	1.00	36.59
ATOM	2627	N	SER	548	40.176	8.906	18.066	1.00	38.91
ATOM	2628	CA	SER	548	39.855	9.212	19.454	1.00	40.88
ATOM	2629	CB	SER	548	40.258	8.050	20.375	1.00	42.68
ATOM	2630	OG	SER	548	41.228	7.208	19.763	1.00	46.74
ATOM	2631	C	SER	548	40.534	10.505	19.902	1.00	40.49
ATOM	2632	O	SER	548	40.013	11.231	20.747	1.00	41.69
ATOM	2633	N	GLN	549	41.691	10.802	19.328	1.00	39.68
ATOM	2634	CA	GLN	549	42.395	12.015	19.686	1.00	39.49
ATOM	2635	CB	GLN	549	43.845	11.956	19.218	1.00	41.25
ATOM	2636	CG	GLN	549	44.736	11.018	20.006	1.00	42.18
ATOM	2637	CD	GLN	549	46.209	11.238	19.706	1.00	42.98
ATOM	2638	OE1	GLN	549	46.922	10.300	19.363	1.00	44.07
ATOM	2639	NE2	GLN	549	46.674	12.479	19.847	1.00	42.49
ATOM	2640	C	GLN	549	41.723	13.222	19.063	1.00	40.07
ATOM	2641	O	GLN	549	41.451	14.213	19.741	1.00	39.72
ATOM	2642	N	THR	550	41.437	13.124	17.770	1.00	41.21
ATOM	2643	CA	THR	550	40.824	14.222	17.036	1.00	43.02
ATOM	2644	CB	THR	550	40.714	13.920	15.515	1.00	43.79
ATOM	2645	CG1	THR	550	40.200	12.595	15.307	1.00	44.92
ATOM	2646	CG2	THR	550	42.069	14.041	14.857	1.00	43.92
ATOM	2647	C	THR	550	39.469	14.641	17.575	1.00	43.65
ATOM	2648	O	THR	550	39.197	15.836	17.716	1.00	43.09
ATOM	2649	N	LYS	551	38.611	13.671	17.871	1.00	45.05
ATOM	2650	CA	LYS	551	37.301	14.027	18.391	1.00	46.81
ATOM	2651	CB	LYS	551	36.265	12.922	18.145	1.00	45.60
ATOM	2652	CG	LYS	551	36.584	11.534	18.617	1.00	44.11
ATOM	2653	CD	LYS	551	35.523	10.578	18.052	1.00	42.52
ATOM	2654	CE	LYS	551	35.569	9.206	18.706	1.00	41.73
ATOM	2655	NZ	LYS	551	34.474	8.315	18.244	1.00	39.62
ATOM	2656	C	LYS	551	37.345	14.523	19.837	1.00	47.87
ATOM	2657	O	LYS	551	36.420	15.198	20.304	1.00	48.23
ATOM	2658	N	GLN	552	38.473	14.275	20.499	1.00	49.00
ATOM	2659	CA	GLN	552	38.699	14.719	21.870	1.00	49.66
ATOM	2660	CB	GLN	552	39.705	13.800	22.555	1.00	51.22
ATOM	2661	CG	GLN	552	40.070	14.232	23.961	1.00	55.29
ATOM	2662	CD	GLN	552	41.365	13.612	24.435	1.00	57.87
ATOM	2663	OE1	GLN	552	41.518	12.383	24.443	1.00	59.24

ATOM	2664	NE2	GLN	552	42.315	14.457	24.827	1.00	59.52
ATOM	2665	C	GLN	552	39.250	16.150	21.837	1.00	50.06
ATOM	2666	O	GLN	552	39.060	16.930	22.776	1.00	49.38
ATOM	2667	N	SER	553	39.944	16.479	20.748	1.00	50.55
ATOM	2668	CA	SER	553	40.532	17.802	20.560	1.00	50.62
ATOM	2669	CB	SER	553	41.660	17.742	19.514	1.00	50.03
ATOM	2670	OG	SER	553	41.169	17.575	18.189	1.00	47.69
ATOM	2671	C	SER	553	39.494	18.833	20.129	1.00	51.44
ATOM	2672	O	SER	553	39.792	20.024	20.048	1.00	52.81
ATOM	2673	N	GLY	554	38.282	18.375	19.840	1.00	52.03
ATOM	2674	CA	GLY	554	37.240	19.282	19.397	1.00	52.43
ATOM	2675	C	GLY	554	37.401	19.638	17.924	1.00	52.57
ATOM	2676	O	GLY	554	36.778	20.581	17.426	1.00	53.51
ATOM	2677	N	GLU	555	38.231	18.874	17.221	1.00	51.69
ATOM	2678	CA	GLU	555	38.470	19.103	15.802	1.00	50.16
ATOM	2679	CB	GLU	555	39.399	18.011	15.259	1.00	51.56
ATOM	2680	CG	GLU	555	40.415	18.498	14.237	1.00	53.15
ATOM	2681	CD	GLU	555	41.455	19.438	14.830	1.00	53.99
ATOM	2682	OE1	GLU	555	42.325	18.955	15.595	1.00	54.91
ATOM	2683	OE2	GLU	555	41.406	20.652	14.521	1.00	53.02
ATOM	2684	C	GLU	555	37.136	19.099	15.047	1.00	47.60
ATOM	2685	O	GLU	555	36.346	18.171	15.193	1.00	48.20
ATOM	2686	N	ASN	556	36.916	20.125	14.226	1.00	45.50
ATOM	2687	CA	ASN	556	35.683	20.303	13.439	1.00	42.96
ATOM	2688	CB	ASN	556	35.796	21.560	12.573	1.00	44.24
ATOM	2689	CG	ASN	556	34.507	22.366	12.529	1.00	45.63
ATOM	2690	OD1	ASN	556	34.544	23.589	12.485	1.00	46.71
ATOM	2691	ND2	ASN	556	33.366	21.687	12.533	1.00	46.27
ATOM	2692	C	ASN	556	35.240	19.117	12.564	1.00	40.45
ATOM	2693	O	ASN	556	34.038	18.830	12.448	1.00	41.36
ATOM	2694	N	PHE	557	36.188	18.477	11.894	1.00	35.01
ATOM	2695	CA	PHE	557	35.874	17.321	11.056	1.00	30.51
ATOM	2696	CB	PHE	557	36.141	17.617	9.575	1.00	26.25
ATOM	2697	CG	PHE	557	35.119	18.516	8.936	1.00	24.10
ATOM	2698	CD1	PHE	557	35.093	19.878	9.212	1.00	23.27
ATOM	2699	CD2	PHE	557	34.184	18.001	8.050	1.00	21.00
ATOM	2700	CE1	PHE	557	34.150	20.710	8.612	1.00	20.85
ATOM	2701	CE2	PHE	557	33.243	18.825	7.450	1.00	18.34
ATOM	2702	CZ	PHE	557	33.225	20.174	7.731	1.00	20.74
ATOM	2703	C	PHE	557	36.809	16.228	11.535	1.00	29.61
ATOM	2704	O	PHE	557	37.739	15.845	10.825	1.00	30.80
ATOM	2705	N	PRO	558	36.557	15.687	12.738	1.00	28.44
ATOM	2706	CD	PRO	558	35.338	15.899	13.535	1.00	27.55
ATOM	2707	CA	PRO	558	37.378	14.633	13.341	1.00	27.40
ATOM	2708	CB	PRO	558	36.580	14.244	14.586	1.00	27.92
ATOM	2709	CG	PRO	558	35.178	14.573	14.212	1.00	28.58
ATOM	2710	C	PRO	558	37.715	13.434	12.459	1.00	25.97
ATOM	2711	O	PRO	558	38.848	12.948	12.490	1.00	25.27
ATOM	2712	N	TYR	559	36.763	12.977	11.652	1.00	23.97
ATOM	2713	CA	TYR	559	37.039	11.836	10.796	1.00	23.89
ATOM	2714	CB	TYR	559	35.753	11.193	10.258	1.00	21.95
ATOM	2715	CG	TYR	559	35.934	9.781	9.769	1.00	21.57
ATOM	2716	CD1	TYR	559	35.891	8.685	10.639	1.00	24.12
ATOM	2717	CE1	TYR	559	36.204	7.339	10.207	1.00	22.12
ATOM	2718	CD2	TYR	559	36.382	9.541	8.461	1.00	22.30
ATOM	2719	CE2	TYR	559	35.696	8.261	8.024	1.00	22.08
ATOM	2720	CZ	TYR	559	35.610	7.199	8.895	1.00	22.68
ATOM	2721	OH	TYR	559	35.966	5.953	8.437	1.00	28.01

ATOM	2722	C	TYR	559	38.002	12.202	9.661	1.00	23.70
ATOM	2723	O	TYR	559	38.932	11.451	9.360	1.00	25.56
ATOM	2724	N	LEU	560	37.819	13.366	9.053	1.00	23.40
ATOM	2725	CA	LEU	560	38.716	13.756	7.965	1.00	22.40
ATOM	2726	CB	LEU	560	38.184	14.979	7.203	1.00	19.29
ATOM	2727	CG	LEU	560	36.905	14.744	6.387	1.00	19.21
ATOM	2728	CD1	LEU	560	36.621	15.965	5.524	1.00	17.94
ATOM	2729	CD2	LEU	560	37.023	13.499	5.508	1.00	16.77
ATOM	2730	C	LEU	560	40.133	14.007	8.475	1.00	21.57
ATOM	2731	O	LEU	560	41.096	13.511	7.896	1.00	22.32
ATOM	2732	N	VAL	561	40.247	14.730	9.587	1.00	21.43
ATOM	2733	CA	VAL	561	41.543	15.049	10.175	1.00	20.86
ATOM	2734	CB	VAL	561	41.404	15.990	11.397	1.00	20.24
ATOM	2735	CG1	VAL	561	42.761	16.265	12.011	1.00	22.08
ATOM	2736	CG2	VAL	561	40.789	17.309	10.972	1.00	20.07
ATOM	2737	C	VAL	561	42.276	13.774	10.566	1.00	21.69
ATOM	2738	O	VAL	561	43.384	13.537	10.103	1.00	22.16
ATOM	2739	N	ALA	562	41.634	12.936	11.379	1.00	22.88
ATOM	2740	CA	ALA	562	42.210	11.672	11.831	1.00	22.13
ATOM	2741	CB	ALA	562	41.248	10.966	12.728	1.00	20.52
ATOM	2742	C	ALA	562	42.580	10.763	10.663	1.00	23.28
ATOM	2743	O	ALA	562	43.571	10.031	10.728	1.00	24.95
ATOM	2744	N	TYR	563	41.787	10.792	9.596	1.00	23.47
ATOM	2745	CA	TYR	563	42.083	9.952	8.443	1.00	24.18
ATOM	2746	CB	TYR	563	40.887	9.861	7.496	1.00	24.43
ATOM	2747	CG	TYR	563	40.962	8.633	6.631	1.00	25.76
ATOM	2748	CD1	TYR	563	40.645	7.376	7.151	1.00	26.28
ATOM	2749	CE1	TYR	563	40.789	6.222	6.386	1.00	27.58
ATOM	2750	CD2	TYR	563	41.418	8.708	5.315	1.00	26.40
ATOM	2751	CE2	TYR	563	41.566	7.560	4.538	1.00	27.19
ATOM	2752	CZ	TYR	563	41.251	6.322	5.081	1.00	27.76
ATOM	2753	OH	TYR	563	41.391	5.193	4.314	1.00	29.58
ATOM	2754	C	TYR	563	43.345	10.426	7.701	1.00	23.93
ATOM	2755	O	TYR	563	44.206	9.612	7.341	1.00	23.21
ATOM	2756	N	GLN	564	43.452	11.736	7.478	1.00	23.24
ATOM	2757	CA	GLN	564	44.631	12.298	6.825	1.00	22.78
ATOM	2758	CB	GLN	564	44.510	13.825	6.675	1.00	21.93
ATOM	2759	CG	GLN	564	45.804	14.539	6.222	1.00	21.73
ATOM	2760	CD	GLN	564	46.209	14.241	4.781	1.00	21.45
ATOM	2761	OE1	GLN	564	45.773	14.928	3.846	1.00	21.98
ATOM	2762	NE2	GLN	564	47.055	13.231	4.595	1.00	18.62
ATOM	2763	C	GLN	564	45.843	11.951	7.689	1.00	22.24
ATOM	2764	O	GLN	564	46.898	11.598	7.170	1.00	22.24
ATOM	2765	N	ALA	565	45.671	12.015	9.006	1.00	22.72
ATOM	2766	CA	ALA	565	46.749	11.700	9.938	1.00	24.32
ATOM	2767	CB	ALA	565	46.330	12.008	11.362	1.00	23.28
ATOM	2768	C	ALA	565	47.138	10.232	9.803	1.00	25.85
ATOM	2769	O	ALA	565	48.324	9.890	9.830	1.00	26.02
ATOM	2770	N	THR	566	46.138	9.377	9.607	1.00	26.56
ATOM	2771	CA	THR	566	46.359	7.939	9.446	1.00	27.00
ATOM	2772	CB	THR	566	45.007	7.215	9.330	1.00	25.94
ATOM	2773	OG1	THR	566	44.338	7.276	10.593	1.00	26.53
ATOM	2774	CG2	THR	566	45.184	5.770	8.926	1.00	25.45
ATOM	2775	C	THR	566	47.223	7.647	8.212	1.00	26.39
ATOM	2776	O	THR	566	48.239	6.951	8.288	1.00	26.71
ATOM	2777	N	VAL	567	46.823	8.205	7.082	1.00	26.66
ATOM	2778	CA	VAL	567	47.533	8.047	5.824	1.00	25.23
ATOM	2779	CB	VAL	567	46.777	8.304	4.704	1.00	24.80

ATOM	2780	CG1	VAL	567	47.633	8.941	3.480	1.00	24.37
ATOM	2781	CG2	VAL	567	45.473	8.053	4.362	1.00	24.95
ATOM	2782	C	VAL	567	48.989	8.519	5.947	1.00	24.66
ATOM	2783	O	VAL	567	49.903	7.867	5.438	1.00	24.50
ATOM	2784	N	CYS	568	49.202	9.622	6.656	1.00	24.76
ATOM	2785	CA	CYS	568	50.544	10.156	6.861	1.00	25.31
ATOM	2786	CB	CYS	568	50.490	11.529	7.546	1.00	24.87
ATOM	2787	SG	CYS	568	49.934	12.883	6.493	1.00	23.18
ATOM	2788	C	CYS	568	51.357	9.188	7.717	1.00	26.58
ATOM	2789	O	CYS	568	52.460	8.797	7.351	1.00	26.47
ATOM	2790	N	ALA	569	50.794	8.776	8.843	1.00	27.17
ATOM	2791	CA	ALA	569	51.484	7.862	9.726	1.00	28.58
ATOM	2792	CB	ALA	569	50.601	7.502	10.904	1.00	28.99
ATOM	2793	C	ALA	569	51.899	6.607	8.967	1.00	30.34
ATOM	2794	O	ALA	569	53.086	6.270	8.921	1.00	31.47
ATOM	2795	N	ARG	570	50.938	5.961	8.308	1.00	30.52
ATOM	2796	CA	ARG	570	51.210	4.732	7.567	1.00	30.59
ATOM	2797	CB	ARG	570	49.918	4.143	6.992	1.00	30.69
ATOM	2798	CG	ARG	570	48.997	3.561	8.054	1.00	30.15
ATOM	2799	CD	ARG	570	47.765	2.913	7.458	1.00	29.12
ATOM	2800	NE	ARG	570	46.828	2.506	8.507	1.00	30.17
ATOM	2801	CZ	ARG	570	45.516	2.374	8.336	1.00	27.42
ATOM	2802	NH1	ARG	570	44.748	1.995	9.347	1.00	29.10
ATOM	2803	NH2	ARG	570	44.966	2.638	7.163	1.00	27.47
ATOM	2804	C	ARG	570	52.253	4.890	6.469	1.00	31.40
ATOM	2805	O	ARG	570	52.902	3.923	6.084	1.00	33.32
ATOM	2806	N	ALA	571	52.390	6.103	5.944	1.00	31.42
ATOM	2807	CA	ALA	571	53.370	6.380	4.901	1.00	29.19
ATOM	2808	CB	ALA	571	52.795	7.363	3.905	1.00	26.97
ATOM	2809	C	ALA	571	54.636	6.960	5.536	1.00	30.02
ATOM	2810	O	ALA	571	55.630	7.179	4.859	1.00	31.04
ATOM	2811	N	GLN	572	54.609	7.157	6.850	1.00	31.02
ATOM	2812	CA	GLN	572	55.727	7.753	7.568	1.00	31.99
ATOM	2813	CB	GLN	572	56.946	6.842	7.579	1.00	35.87
ATOM	2814	CG	GLN	572	56.830	5.689	8.542	1.00	41.94
ATOM	2815	CD	GLN	572	58.170	5.040	8.801	1.00	45.72
ATOM	2816	OE1	GLN	572	58.562	4.819	9.954	1.00	47.02
ATOM	2817	NE2	GLN	572	58.894	4.740	7.726	1.00	48.15
ATOM	2818	C	GLN	572	56.071	9.093	6.935	1.00	30.48
ATOM	2819	O	GLN	572	57.235	9.489	6.880	1.00	30.24
ATOM	2820	N	ALA	573	55.029	9.765	6.451	1.00	28.34
ATOM	2821	CA	ALA	573	55.114	11.072	5.814	1.00	26.25
ATOM	2822	CB	ALA	573	54.253	11.084	4.537	1.00	24.36
ATOM	2823	C	ALA	573	54.601	12.113	6.822	1.00	25.50
ATOM	2824	O	ALA	573	53.844	11.783	7.744	1.00	24.77
ATOM	2825	N	PRO	574	55.049	13.370	6.699	1.00	24.64
ATOM	2826	CD	PRO	574	56.068	13.892	5.771	1.00	24.05
ATOM	2827	CA	PRO	574	54.595	14.404	7.633	1.00	24.57
ATOM	2828	CB	PRO	574	55.675	15.471	7.500	1.00	25.21
ATOM	2829	CG	PRO	574	56.036	15.383	6.042	1.00	26.61
ATOM	2830	C	PRO	574	53.227	14.957	7.253	1.00	25.52
ATOM	2831	O	PRO	574	52.784	14.813	6.107	1.00	25.99
ATOM	2832	N	PRO	575	52.525	15.580	8.212	1.00	25.30
ATOM	2833	CD	PRO	575	52.893	15.792	9.622	1.00	24.49
ATOM	2834	CA	PRO	575	51.202	16.146	7.926	1.00	25.44
ATOM	2835	CB	PRO	575	50.717	16.584	9.339	1.00	25.55
ATOM	2836	CG	PRO	575	51.989	16.927	10.022	1.00	25.38
ATOM	2837	C	PRO	575	51.327	17.324	6.955	1.00	25.27

ATOM	2838	O	PRO	575	52.439	17.751	6.630	1.00	24.04
ATOM	2839	N	PRO	576	50.190	17.827	6.440	1.00	25.82
ATOM	2840	CD	PRO	576	48.829	17.300	6.637	1.00	24.51
ATOM	2841	CA	PRO	576	50.171	18.952	5.501	1.00	26.20
ATOM	2842	CB	PRO	576	48.686	19.236	5.357	1.00	24.96
ATOM	2843	CG	PRO	576	48.099	17.876	5.460	1.00	25.27
ATOM	2844	C	PRO	576	50.935	20.158	6.031	1.00	27.89
ATOM	2845	O	PRO	576	51.529	20.921	5.262	1.00	28.06
ATOM	2846	N	SER	577	50.893	20.333	7.345	1.00	29.44
ATOM	2847	CA	SER	577	51.599	21.415	8.012	1.00	30.58
ATOM	2848	CB	SER	577	50.800	22.720	7.946	1.00	29.32
ATOM	2849	OG	SER	577	49.630	22.650	8.739	1.00	29.45
ATOM	2850	C	SER	577	51.777	20.963	9.452	1.00	32.15
ATOM	2851	O	SER	577	51.410	19.839	9.801	1.00	31.77
ATOM	2852	N	TRP	578	52.371	21.819	10.276	1.00	34.52
ATOM	2853	CA	TRP	578	52.580	21.500	11.680	1.00	35.77
ATOM	2854	CB	TRP	578	54.069	21.540	12.040	1.00	36.18
ATOM	2855	CG	TRP	578	54.784	20.303	11.588	1.00	36.28
ATOM	2856	CD2	TRP	578	54.612	18.983	12.111	1.00	36.36
ATOM	2857	CE2	TRP	578	55.441	18.121	11.353	1.00	35.89
ATOM	2858	CE3	TRP	578	53.835	18.443	13.148	1.00	35.12
ATOM	2859	CD1	TRP	578	55.691	20.196	10.564	1.00	35.71
ATOM	2860	NE1	TRP	578	56.086	18.887	10.418	1.00	35.51
ATOM	2861	CZ2	TRP	578	55.513	16.746	11.599	1.00	35.54
ATOM	2862	CZ3	TRP	578	53.907	17.078	13.391	1.00	35.54
ATOM	2863	CH2	TRP	578	54.741	16.244	12.619	1.00	36.06
ATOM	2864	C	TRP	578	51.761	22.431	12.555	1.00	35.97
ATOM	2865	O	TRP	578	52.179	22.832	13.635	1.00	36.76
ATOM	2866	N	ASP	579	50.595	22.800	12.051	1.00	36.49
ATOM	2867	CA	ASP	579	49.694	23.656	12.786	1.00	38.09
ATOM	2868	CB	ASP	579	48.710	24.314	11.819	1.00	41.72
ATOM	2869	CG	ASP	579	49.409	25.243	10.817	1.00	45.89
ATOM	2870	OD1	ASP	579	49.175	25.102	9.595	1.00	48.85
ATOM	2871	OD2	ASP	579	50.197	26.119	11.248	1.00	48.08
ATOM	2872	C	ASP	579	48.999	22.742	13.792	1.00	37.56
ATOM	2873	O	ASP	579	48.998	21.528	13.606	1.00	38.03
ATOM	2874	N	ALA	580	48.419	23.316	14.847	1.00	36.79
ATOM	2875	CA	ALA	580	47.748	22.552	15.915	1.00	35.50
ATOM	2876	CB	ALA	580	46.956	23.496	16.810	1.00	36.40
ATOM	2877	C	ALA	580	46.856	21.391	15.470	1.00	34.02
ATOM	2878	O	ALA	580	46.700	20.404	16.188	1.00	32.85
ATOM	2879	N	MET	581	46.272	21.520	14.285	1.00	33.63
ATOM	2880	CA	MET	581	45.401	20.492	13.740	1.00	32.54
ATOM	2881	CB	MET	581	44.908	20.902	12.348	1.00	32.51
ATOM	2882	CG	MET	581	44.043	19.857	11.656	1.00	31.86
ATOM	2883	SD	MET	581	43.448	20.404	10.057	1.00	33.21
ATOM	2884	CE	MET	581	42.419	21.765	10.534	1.00	34.37
ATOM	2885	C	MET	581	46.119	19.158	13.636	1.00	32.20
ATOM	2886	O	MET	581	45.470	18.113	13.609	1.00	33.12
ATOM	2887	N	TRP	582	47.450	19.194	13.591	1.00	30.73
ATOM	2888	CA	TRP	582	48.246	17.979	13.455	1.00	29.56
ATOM	2889	CB	TRP	582	49.078	18.060	12.172	1.00	25.83
ATOM	2890	CG	TRP	582	48.252	18.490	10.972	1.00	22.26
ATOM	2891	CD2	TRP	582	47.205	17.743	10.330	1.00	19.39
ATOM	2892	CE2	TRP	582	46.672	18.563	9.319	1.00	18.29
ATOM	2893	CE3	TRP	582	45.666	16.461	10.515	1.00	18.37
ATOM	2894	CD1	TRP	582	48.312	19.690	10.331	1.00	19.79
ATOM	2895	NE1	TRP	582	47.367	19.744	9.345	1.00	19.82

ATOM	2896	CZ2	TRP	582	45.620	18.148	8.490	1.00	16.85
ATOM	2897	CZ3	TRP	582	45.623	16.047	9.693	1.00	16.11
ATOM	2898	CH2	TRP	582	45.111	16.891	8.694	1.00	17.32
ATOM	2899	C	TRP	582	49.121	17.630	14.661	1.00	31.31
ATOM	2900	O	TRP	582	50.215	17.097	14.519	1.00	31.41
ATOM	2901	N	ALA	583	48.589	17.866	15.856	1.00	34.62
ATOM	2902	CA	ALA	583	49.285	17.575	17.107	1.00	34.61
ATOM	2903	CB	ALA	583	48.493	18.145	18.283	1.00	34.87
ATOM	2904	C	ALA	583	49.496	16.075	17.295	1.00	34.99
ATOM	2905	O	ALA	583	50.489	15.646	17.877	1.00	35.31
ATOM	2906	N	CYS	584	48.560	15.282	16.788	1.00	37.04
ATOM	2907	CA	CYS	584	48.610	13.815	16.893	1.00	38.08
ATOM	2908	CB	CYS	584	47.396	13.199	16.182	1.00	37.55
ATOM	2909	SG	CYS	584	47.130	13.868	14.512	1.00	40.22
ATOM	2910	C	CYS	584	49.886	13.200	16.317	1.00	37.89
ATOM	2911	O	CYS	584	50.375	12.178	16.809	1.00	37.62
ATOM	2912	N	LEU	585	50.422	13.835	15.279	1.00	37.89
ATOM	2913	CA	LEU	585	51.616	13.339	14.604	1.00	37.24
ATOM	2914	CB	LEU	585	51.506	13.590	13.099	1.00	34.72
ATOM	2915	CG	LEU	585	50.359	12.817	12.447	1.00	33.11
ATOM	2916	CD1	LEU	585	50.194	13.205	10.994	1.00	32.42
ATOM	2917	CD2	LEU	585	50.624	11.328	12.586	1.00	33.32
ATOM	2918	C	LEU	585	52.913	13.916	15.122	1.00	37.69
ATOM	2919	O	LEU	585	53.967	13.659	14.549	1.00	38.68
ATOM	2920	N	ILE	586	52.844	14.667	16.215	1.00	38.37
ATOM	2921	CA	ILE	586	54.033	15.286	16.776	1.00	39.55
ATOM	2922	CB	ILE	586	53.675	16.366	17.816	1.00	38.52
ATOM	2923	CG2	ILE	586	54.915	16.799	18.593	1.00	37.57
ATOM	2924	CG1	ILE	586	53.067	17.575	17.101	1.00	38.01
ATOM	2925	CD1	ILE	586	52.671	18.705	18.018	1.00	37.82
ATOM	2926	C	ILE	586	55.015	14.277	17.355	1.00	41.37
ATOM	2927	O	ILE	586	56.191	14.274	16.985	1.00	42.88
ATOM	2928	N	ALA	587	54.528	13.391	18.215	1.00	41.55
ATOM	2929	CA	ALA	587	55.381	12.390	18.832	1.00	41.50
ATOM	2930	CB	ALA	587	54.544	11.442	19.665	1.00	42.38
ATOM	2931	C	ALA	587	56.214	11.606	17.810	1.00	42.23
ATOM	2932	O	ALA	587	57.358	11.236	18.089	1.00	43.74
ATOM	2933	N	LEU	588	55.644	11.375	16.628	1.00	41.27
ATOM	2934	CA	LEU	588	56.315	10.627	15.561	1.00	39.52
ATOM	2935	CB	LEU	588	55.270	9.940	14.678	1.00	39.86
ATOM	2936	CG	LEU	588	54.315	8.889	15.240	1.00	38.47
ATOM	2937	CD1	LEU	588	53.206	8.640	14.235	1.00	36.97
ATOM	2938	CD2	LEU	588	55.072	7.609	15.545	1.00	37.35
ATOM	2939	C	LEU	588	57.190	11.497	14.656	1.00	39.04
ATOM	2940	O	LEU	588	58.020	10.984	13.912	1.00	36.99
ATOM	2941	N	LYS	589	56.999	12.809	14.742	1.00	40.00
ATOM	2942	CA	LYS	589	57.701	13.800	13.922	1.00	42.08
ATOM	2943	CB	LYS	589	57.711	15.158	14.635	1.00	40.84
ATOM	2944	CG	LYS	589	58.259	16.282	13.795	1.00	41.90
ATOM	2945	CD	LYS	589	57.780	17.626	14.304	1.00	43.78
ATOM	2946	CE	LYS	589	58.264	18.756	13.414	1.00	44.18
ATOM	2947	NZ	LYS	589	57.675	20.058	13.824	1.00	46.71
ATOM	2948	C	LYS	589	59.099	13.460	13.368	1.00	43.12
ATOM	2949	O	LYS	589	59.343	13.595	12.162	1.00	43.36
ATOM	2950	N	PRO	590	60.026	13.013	14.230	1.00	43.51
ATOM	2951	CD	PRO	590	59.933	12.911	15.698	1.00	44.56
ATOM	2952	CA	PRO	590	61.378	12.572	13.778	1.00	42.92
ATOM	2953	CB	PRO	590	62.039	12.177	15.059	1.00	44.20

ATOM	2954	CG	PRO	590	61.380	13.008	16.112	1.00	44.80
ATOM	2955	C	PRO	590	61.432	11.598	12.700	1.00	42.62
ATOM	2956	O	PRO	590	62.368	11.558	11.901	1.00	44.16
ATOM	2957	N	THR	591	60.443	10.716	12.697	1.00	40.90
ATOM	2958	CA	THR	591	60.386	9.625	11.735	1.00	38.82
ATOM	2959	CB	THR	591	59.742	8.390	12.393	1.00	40.84
ATOM	2960	OG1	THR	591	58.390	8.691	12.775	1.00	41.16
ATOM	2961	CG2	THR	591	60.531	7.999	13.643	1.00	40.40
ATOM	2962	C	THR	591	59.637	9.953	10.441	1.00	36.37
ATOM	2963	O	THR	591	59.770	9.249	9.438	1.00	35.64
ATOM	2964	N	LEU	592	58.844	11.016	10.467	1.00	35.52
ATOM	2965	CA	LEU	592	58.054	11.415	9.308	1.00	32.95
ATOM	2966	CB	LEU	592	56.904	12.330	9.737	1.00	31.23
ATOM	2967	CG	LEU	592	55.935	11.656	10.719	1.00	30.46
ATOM	2968	CD1	LEU	592	54.765	12.565	11.025	1.00	30.71
ATOM	2969	CD2	LEU	592	55.438	10.341	10.145	1.00	28.34
ATOM	2970	C	LEU	592	58.945	12.090	8.293	1.00	32.65
ATOM	2971	O	LEU	592	59.561	13.116	8.579	1.00	31.57
ATOM	2972	N	HIS	593	58.998	11.508	7.100	1.00	33.01
ATOM	2973	CA	HIS	593	59.840	12.005	6.016	1.00	33.45
ATOM	2974	CB	HIS	593	61.103	11.140	5.916	1.00	36.56
ATOM	2975	CG	HIS	593	60.814	9.677	5.743	1.00	40.30
ATOM	2976	CD2	HIS	593	60.734	8.908	4.632	1.00	41.91
ATOM	2977	ND1	HIS	593	60.502	8.849	6.801	1.00	42.01
ATOM	2978	CE1	HIS	593	60.239	7.634	6.351	1.00	41.87
ATOM	2979	NE2	HIS	593	60.371	7.643	5.037	1.00	42.34
ATOM	2980	C	HIS	593	59.133	11.968	4.670	1.00	31.17
ATOM	2981	O	HIS	593	58.321	11.084	4.398	1.00	30.16
ATOM	2982	N	GLY	594	59.478	12.925	3.821	1.00	30.14
ATOM	2983	CA	GLY	594	58.907	12.975	2.490	1.00	27.59
ATOM	2984	C	GLY	594	57.747	13.918	2.282	1.00	24.95
ATOM	2985	O	GLY	594	57.465	14.775	3.123	1.00	26.12
ATOM	2986	N	PRO	595	57.093	13.815	1.119	1.00	22.45
ATOM	2987	CD	PRO	595	57.443	12.914	0.005	1.00	21.56
ATOM	2988	CA	PRO	595	55.951	14.652	0.776	1.00	21.39
ATOM	2989	CB	PRO	595	55.888	14.516	-0.739	1.00	21.51
ATOM	2990	CG	PRO	595	56.283	13.091	-0.953	1.00	21.07
ATOM	2991	C	PRO	595	54.684	14.117	1.443	1.00	21.15
ATOM	2992	O	PRO	595	54.562	12.927	1.741	1.00	21.34
ATOM	2993	N	THR	596	53.752	15.017	1.695	1.00	20.85
ATOM	2994	CA	THR	596	52.489	14.685	2.314	1.00	19.78
ATOM	2995	CB	THR	596	51.855	15.958	2.914	1.00	18.44
ATOM	2996	OG1	THR	596	52.742	16.520	3.890	1.00	18.54
ATOM	2997	CG2	THR	596	50.512	15.640	3.552	1.00	17.29
ATOM	2998	C	THR	596	51.499	14.121	1.304	1.00	19.38
ATOM	2999	O	THR	596	51.308	14.712	0.233	1.00	19.92
ATOM	3000	N	PRO	597	50.977	12.901	1.551	1.00	19.28
ATOM	3001	CD	PRO	597	51.461	11.862	2.478	1.00	18.63
ATOM	3002	CA	PRO	597	49.997	12.351	0.607	1.00	19.90
ATOM	3003	CB	PRO	597	49.972	10.863	0.970	1.00	19.83
ATOM	3004	CG	PRO	597	50.380	10.840	2.410	1.00	19.57
ATOM	3005	C	PRO	597	48.671	13.092	0.927	1.00	20.50
ATOM	3006	O	PRO	597	47.891	12.680	1.790	1.00	20.99
ATOM	3007	N	LEU	598	48.501	14.252	0.294	1.00	18.90
ATOM	3008	CA	LEU	598	47.355	15.120	0.510	1.00	17.83
ATOM	3009	CB	LEU	598	47.614	16.493	-0.128	1.00	17.96
ATOM	3010	CG	LEU	598	46.722	17.655	0.314	1.00	18.91
ATOM	3011	CD1	LEU	598	46.943	17.896	1.792	1.00	16.89

ATOM	3012	CD2	LEU	598	47.011	18.916	-0.490	1.00	16.71
ATOM	3013	C	LEU	598	46.037	14.542	0.010	1.00	17.19
ATOM	3014	O	LEU	598	45.862	14.285	-1.187	1.00	17.59
ATOM	3015	N	LEU	599	45.097	14.378	0.935	1.00	15.70
ATOM	3016	CA	LEU	599	43.801	13.823	0.598	1.00	15.41
ATOM	3017	CB	LEU	599	43.236	13.034	1.782	1.00	14.25
ATOM	3018	CG	LEU	599	44.071	11.861	2.304	1.00	14.47
ATOM	3019	CD1	LEU	599	43.268	11.092	3.331	1.00	11.46
ATOM	3020	CD2	LEU	599	44.500	10.944	1.165	1.00	12.30
ATOM	3021	C	LEU	599	42.832	14.907	0.188	1.00	15.60
ATOM	3022	O	LEU	599	42.063	14.739	-0.743	1.00	14.98
ATOM	3023	N	TYR	600	42.889	16.022	0.902	1.00	16.33
ATOM	3024	CA	TYR	600	42.025	17.178	0.675	1.00	16.87
ATOM	3025	CB	TYR	600	40.607	16.876	1.177	1.00	16.11
ATOM	3026	CG	TYR	600	40.567	15.864	2.303	1.00	15.17
ATOM	3027	CD1	TYR	600	41.172	16.124	3.536	1.00	15.04
ATOM	3028	CE1	TYR	600	41.198	15.163	4.546	1.00	15.31
ATOM	3029	CD2	TYR	600	39.980	14.622	2.112	1.00	15.05
ATOM	3030	CE2	TYR	600	39.997	13.657	3.112	1.00	16.28
ATOM	3031	CZ	TYR	600	40.607	13.931	4.323	1.00	15.83
ATOM	3032	OH	TYR	600	40.623	12.953	5.295	1.00	18.80
ATOM	3033	C	TYR	600	42.644	18.279	1.516	1.00	16.31
ATOM	3034	O	TYR	600	43.624	18.025	2.212	1.00	17.03
ATOM	3035	N	ARG	601	42.083	19.485	1.480	1.00	17.91
ATOM	3036	CA	ARG	601	42.623	20.578	2.287	1.00	19.15
ATOM	3037	CB	ARG	601	42.991	21.775	1.407	1.00	19.16
ATOM	3038	CG	ARG	601	43.949	21.415	0.298	1.00	21.99
ATOM	3039	CD	ARG	601	44.411	22.615	-0.487	1.00	24.32
ATOM	3040	NE	ARG	601	45.189	22.200	-1.649	1.00	27.46
ATOM	3041	CZ	ARG	601	46.317	22.783	-2.052	1.00	29.91
ATOM	3042	NH1	ARG	601	46.954	22.328	-3.127	1.00	29.79
ATOM	3043	NH2	ARG	601	46.813	23.819	-1.385	1.00	29.28
ATOM	3044	C	ARG	601	41.688	21.004	3.420	1.00	20.23
ATOM	3045	O	ARG	601	40.501	21.273	3.208	1.00	20.27
ATOM	3046	N	LEU	602	42.237	21.035	4.630	1.00	21.19
ATOM	3047	CA	LEU	602	41.496	21.427	5.821	1.00	22.38
ATOM	3048	CB	LEU	602	41.437	20.264	6.809	1.00	22.22
ATOM	3049	CG	LEU	602	40.807	18.965	6.306	1.00	23.52
ATOM	3050	CD1	LEU	602	40.914	17.913	7.390	1.00	22.77
ATOM	3051	CD2	LEU	602	39.349	19.186	5.895	1.00	23.14
ATOM	3052	C	LEU	602	42.228	22.594	6.468	1.00	23.77
ATOM	3053	O	LEU	602	41.820	23.108	7.511	1.00	24.94
ATOM	3054	N	GLY	603	43.318	23.003	5.830	1.00	25.45
ATOM	3055	CA	GLY	603	44.131	24.087	6.330	1.00	25.21
ATOM	3056	C	GLY	603	45.240	24.352	5.339	1.00	26.57
ATOM	3057	O	GLY	603	45.160	23.924	4.183	1.00	26.29
ATOM	3058	N	ALA	604	46.293	25.021	5.796	1.00	27.24
ATOM	3059	CA	ALA	604	47.417	25.362	4.934	1.00	27.36
ATOM	3060	CB	ALA	604	48.215	26.499	5.554	1.00	27.18
ATOM	3061	C	ALA	604	48.315	24.164	4.684	1.00	26.80
ATOM	3062	O	ALA	604	48.598	23.395	5.603	1.00	26.71
ATOM	3063	N	VAL	605	48.729	23.990	3.431	1.00	28.18
ATOM	3064	CA	VAL	605	49.615	22.892	3.059	1.00	29.48
ATOM	3065	CB	VAL	605	49.089	22.064	1.812	1.00	28.74
ATOM	3066	CG1	VAL	605	47.642	21.658	2.015	1.00	28.64
ATOM	3067	CG2	VAL	605	49.221	22.825	0.518	1.00	29.95
ATOM	3068	C	VAL	605	51.000	23.487	2.821	1.00	30.10
ATOM	3069	O	VAL	605	51.255	24.133	1.907	1.00	30.39

ATOM	3070	N	GLN	606	51.863	23.357	3.818	1.00	31.14
ATOM	3071	CA	GLN	606	53.213	23.897	3.720	1.00	32.44
ATOM	3072	CB	GLN	606	53.627	24.481	5.068	1.00	34.05
ATOM	3073	CG	GLN	606	52.846	25.750	5.412	1.00	38.82
ATOM	3074	CD	GLN	606	52.595	25.915	6.899	1.00	41.93
ATOM	3075	OE1	GLN	606	51.501	26.294	7.316	1.00	44.45
ATOM	3076	NE2	GLN	606	53.605	25.625	7.710	1.00	43.43
ATOM	3077	C	GLN	606	54.249	22.900	3.200	1.00	31.71
ATOM	3078	O	GLN	606	55.117	23.251	2.399	1.00	32.38
ATOM	3079	N	ASN	607	54.143	21.652	3.636	1.00	30.92
ATOM	3080	CA	ASN	607	55.074	20.616	3.208	1.00	29.53
ATOM	3081	CB	ASN	607	54.861	19.351	4.047	1.00	31.91
ATOM	3082	CG	ASN	607	55.911	18.281	3.778	1.00	34.41
ATOM	3083	OD1	ASN	607	57.109	18.580	3.692	1.00	35.38
ATOM	3084	ND2	ASN	607	55.471	17.035	3.626	1.00	33.25
ATOM	3085	C	ASN	607	54.892	20.287	1.728	1.00	28.03
ATOM	3086	O	ASN	607	53.937	20.733	1.089	1.00	27.96
ATOM	3087	N	GLU	608	55.852	19.566	1.164	1.00	26.45
ATOM	3088	CA	GLU	608	55.755	19.146	-0.227	1.00	25.62
ATOM	3089	CB	GLU	608	57.023	18.420	-0.663	1.00	28.49
ATOM	3090	CG	GLU	608	58.214	19.314	-0.845	1.00	33.96
ATOM	3091	CD	GLU	608	59.497	18.528	-0.996	1.00	38.84
ATOM	3092	OE1	GLU	608	59.482	17.495	-1.711	1.00	40.73
ATOM	3093	OE2	GLU	608	60.515	18.941	-0.388	1.00	40.03
ATOM	3094	C	GLU	608	54.604	18.168	-0.242	1.00	22.39
ATOM	3095	O	GLU	608	54.364	17.499	0.754	1.00	22.12
ATOM	3096	N	VAL	609	53.947	18.036	-1.384	1.00	21.16
ATOM	3097	CA	VAL	609	52.803	17.147	-1.525	1.00	19.97
ATOM	3098	CB	VAL	609	51.526	17.971	-1.943	1.00	18.69
ATOM	3099	CG1	VAL	609	50.343	17.049	-2.263	1.00	18.90
ATOM	3100	CG2	VAL	609	51.136	18.937	-0.851	1.00	17.99
ATOM	3101	C	VAL	609	53.020	16.099	-2.607	1.00	19.62
ATOM	3102	O	VAL	609	53.767	16.337	-3.560	1.00	19.53
ATOM	3103	N	THR	610	52.413	14.926	-2.419	1.00	19.46
ATOM	3104	CA	THR	610	52.412	13.872	-3.430	1.00	20.82
ATOM	3105	CB	THR	610	53.156	12.556	-3.003	1.00	21.42
ATOM	3106	OG1	THR	610	53.151	11.639	-4.108	1.00	21.70
ATOM	3107	CG2	THR	610	52.507	11.877	-1.806	1.00	20.08
ATOM	3108	C	THR	610	50.917	13.607	-3.657	1.00	21.22
ATOM	3109	O	THR	610	50.105	13.807	-2.743	1.00	22.98
ATOM	3110	N	LEU	611	50.541	13.278	-4.890	1.00	21.98
ATOM	3111	CA	LEU	611	49.145	12.981	-5.239	1.00	21.98
ATOM	3112	CB	LEU	611	48.648	13.895	-6.369	1.00	20.70
ATOM	3113	CG	LEU	611	48.629	15.415	-6.175	1.00	22.00
ATOM	3114	CD1	LEU	611	47.817	16.058	-7.299	1.00	20.18
ATOM	3115	CD2	LEU	611	48.018	15.759	-4.815	1.00	22.59
ATOM	3116	C	LEU	611	49.030	11.528	-5.700	1.00	22.41
ATOM	3117	O	LEU	611	48.086	11.155	-6.389	1.00	24.23
ATOM	3118	N	THR	612	49.997	10.709	-5.321	1.00	23.19
ATOM	3119	CA	THR	612	50.002	9.319	-5.732	1.00	25.23
ATOM	3120	CB	THR	612	51.449	8.834	-5.995	1.00	27.01
ATOM	3121	OG1	THR	612	52.242	8.995	-4.805	1.00	29.09
ATOM	3122	CG2	THR	612	52.079	9.633	-7.127	1.00	27.28
ATOM	3123	C	THR	612	49.331	8.350	-4.765	1.00	24.95
ATOM	3124	O	THR	612	49.217	7.168	-5.072	1.00	25.66
ATOM	3125	N	HIS	613	48.904	8.816	-3.595	1.00	24.14
ATOM	3126	CA	HIS	613	48.283	7.898	-2.653	1.00	23.56
ATOM	3127	CB	HIS	613	48.080	8.555	-1.292	1.00	21.38

ATOM	3128	CG	HIS	613	47.870	7.579	-0.171	1.00	21.58
ATOM	3129	CD2	HIS	613	48.699	7.162	0.814	1.00	21.05
ATOM	3130	ND1	HIS	613	46.680	6.909	0.026	1.00	20.95
ATOM	3131	CE1	HIS	613	46.788	6.118	1.080	1.00	18.99
ATOM	3132	NE2	HIS	613	48.002	6.255	1.577	1.00	19.71
ATOM	3133	C	HIS	613	46.962	7.381	-3.225	1.00	24.95
ATOM	3134	O	HIS	613	46.211	8.132	-3.855	1.00	24.56
ATOM	3135	N	PRO	614	46.683	6.074	-3.047	1.00	25.96
ATOM	3136	CD	PRO	614	47.577	5.083	-2.412	1.00	25.46
ATOM	3137	CA	PRO	614	45.455	5.430	-3.537	1.00	25.84
ATOM	3138	CB	PRO	614	45.526	4.051	-2.884	1.00	25.79
ATOM	3139	CG	PRO	614	46.989	3.774	-2.849	1.00	26.21
ATOM	3140	C	PRO	614	44.168	6.182	-3.137	1.00	26.01
ATOM	3141	O	PRO	614	43.253	6.346	-3.946	1.00	26.99
ATOM	3142	N	ILE	615	44.114	6.643	-1.890	1.00	25.62
ATOM	3143	CA	ILE	615	42.959	7.379	-1.383	1.00	25.23
ATOM	3144	CB	ILE	615	43.075	7.635	0.132	1.00	26.29
ATOM	3145	CG2	ILE	615	41.823	8.358	0.644	1.00	25.16
ATOM	3146	CG1	ILE	615	43.264	6.306	0.873	1.00	24.79
ATOM	3147	CD1	ILE	615	42.158	5.291	0.603	1.00	25.74
ATOM	3148	C	ILE	615	42.766	8.699	-2.127	1.00	25.02
ATOM	3149	O	ILE	615	41.641	9.075	-2.449	1.00	24.98
ATOM	3150	N	THR	616	43.870	9.388	-2.409	1.00	24.97
ATOM	3151	CA	THR	616	43.838	10.654	-3.142	1.00	24.03
ATOM	3152	CB	THR	616	45.268	11.208	-3.307	1.00	21.36
ATOM	3153	OG1	THR	616	45.880	11.313	-2.023	1.00	19.82
ATOM	3154	CG2	THR	616	45.255	12.573	-3.946	1.00	22.30
ATOM	3155	C	THR	616	43.234	10.403	-4.531	1.00	25.54
ATOM	3156	O	THR	616	42.312	11.107	-4.970	1.00	25.06
ATOM	3157	N	LYS	617	43.745	9.374	-5.205	1.00	26.21
ATOM	3158	CA	LYS	617	43.268	9.013	-6.532	1.00	26.68
ATOM	3159	CB	LYS	617	44.103	7.865	-7.106	1.00	29.57
ATOM	3160	CG	LYS	617	45.601	8.150	-7.174	1.00	32.92
ATOM	3161	CD	LYS	617	46.125	8.036	-8.593	1.00	36.18
ATOM	3162	CE	LYS	617	45.459	9.068	-9.512	1.00	39.50
ATOM	3163	NZ	LYS	617	45.780	8.867	-10.963	1.00	39.79
ATOM	3164	C	LYS	617	41.789	8.630	-6.469	1.00	25.76
ATOM	3165	O	LYS	617	41.023	8.968	-7.375	1.00	23.91
ATOM	3166	N	TYR	618	41.401	7.935	-5.397	1.00	25.82
ATOM	3167	CA	TYR	618	40.010	7.518	-5.180	1.00	26.33
ATOM	3168	CB	TYR	618	39.884	6.701	-3.883	1.00	28.26
ATOM	3169	CG	TYR	618	38.441	6.394	-3.504	1.00	32.04
ATOM	3170	CD1	TYR	618	37.768	5.307	-4.081	1.00	33.48
ATOM	3171	CE1	TYR	618	36.423	5.049	-3.804	1.00	32.78
ATOM	3172	CD2	TYR	618	37.725	7.221	-2.624	1.00	31.35
ATOM	3173	CE2	TYR	618	36.372	6.971	-2.339	1.00	31.99
ATOM	3174	CZ	TYR	618	35.735	5.880	-2.938	1.00	33.67
ATOM	3175	OH	TYR	618	34.421	5.588	-2.668	1.00	34.74
ATOM	3176	C	TYR	618	39.091	8.740	-5.086	1.00	26.08
ATOM	3177	O	TYR	618	38.135	8.871	-5.850	1.00	24.27
ATOM	3178	N	ILE	619	39.395	9.637	-4.148	1.00	26.53
ATOM	3179	CA	ILE	619	38.592	10.840	-3.952	1.00	26.78
ATOM	3180	CB	ILE	619	39.110	11.695	-2.771	1.00	26.09
ATOM	3181	CG2	ILE	619	38.201	12.890	-2.554	1.00	27.00
ATOM	3182	CG1	ILE	619	39.114	10.858	-1.484	1.00	24.87
ATOM	3183	CD1	ILE	619	39.696	11.585	-0.275	1.00	23.06
ATOM	3184	C	ILE	619	38.531	11.669	-5.232	1.00	27.63
ATOM	3185	O	ILE	619	37.510	12.299	-5.517	1.00	28.55

ATOM	3186	N	MET	620	39.603	11.635	-6.020	1.00	28.31
ATOM	3187	CA	MET	620	39.642	12.367	-7.281	1.00	29.16
ATOM	3188	CB	MET	620	41.047	12.339	-7.888	1.00	30.86
ATOM	3189	CG	MET	620	42.068	13.180	-7.133	1.00	31.31
ATOM	3190	SD	MET	620	43.700	13.152	-7.887	1.00	33.66
ATOM	3191	CE	MET	620	43.745	14.717	-8.555	1.00	34.32
ATOM	3192	C	MET	620	38.625	11.813	-8.274	1.00	29.85
ATOM	3193	O	MET	620	38.040	12.563	-9.048	1.00	29.99
ATOM	3194	N	THR	621	38.397	10.504	-8.248	1.00	31.58
ATOM	3195	CA	THR	621	37.412	9.909	-9.146	1.00	33.23
ATOM	3196	CB	THR	621	37.505	8.351	-9.182	1.00	34.83
ATOM	3197	OG1	THR	621	37.348	7.801	-7.865	1.00	34.63
ATOM	3198	CG2	THR	621	38.853	7.918	-9.741	1.00	34.93
ATOM	3199	C	THR	621	36.008	10.355	-8.727	1.00	33.69
ATOM	3200	O	THR	621	35.089	10.387	-9.539	1.00	32.60
ATOM	3201	N	CYS	622	35.860	10.705	-7.449	1.00	35.29
ATOM	3202	CA	CYS	622	34.582	11.166	-6.915	1.00	36.11
ATOM	3203	CB	CYS	622	34.584	11.148	-5.379	1.00	34.25
ATOM	3204	SG	CYS	622	34.541	9.474	-4.630	1.00	34.81
ATOM	3205	C	CYS	622	34.282	12.565	-7.434	1.00	37.34
ATOM	3206	O	CYS	622	33.124	12.980	-7.498	1.00	38.25
ATOM	3207	N	MET	623	35.329	13.284	-7.823	1.00	38.28
ATOM	3208	CA	MET	623	35.161	14.626	-8.352	1.00	40.10
ATOM	3209	CB	MET	623	36.477	15.399	-8.297	1.00	38.66
ATOM	3210	CG	MET	623	37.160	15.447	-6.952	1.00	38.37
ATOM	3211	SD	MET	623	36.295	16.417	-5.730	1.00	38.37
ATOM	3212	CE	MET	623	36.561	15.423	-4.310	1.00	38.68
ATOM	3213	C	MET	623	34.701	14.559	-9.809	1.00	42.69
ATOM	3214	O	MET	623	33.953	15.425	-10.263	1.00	44.25
ATOM	3215	N	SER	624	35.169	13.544	-10.539	1.00	44.54
ATOM	3216	CA	SER	624	34.843	13.373	-11.959	1.00	45.95
ATOM	3217	CB	SER	624	35.862	12.432	-12.624	1.00	46.09
ATOM	3218	OG	SER	624	36.043	11.237	-11.879	1.00	45.68
ATOM	3219	C	SER	624	33.408	12.937	-12.294	1.00	46.50
ATOM	3220	O	SER	624	32.901	11.984	-11.658	1.00	48.12

SULFATE ION COORDINATES

		Atom Type	Resid	#	X	Y	Z	OCC	B
ATOM	3221	S	SO4	1001	8.646	28.709	22.190	1.00	32.01
ATOM	3222	O1	SO4	1001	9.006	27.263	22.094	1.00	35.92
ATOM	3223	O2	SO4	1001	8.328	28.982	23.610	1.00	33.43
ATOM	3224	O3	SO4	1001	9.821	29.520	21.744	1.00	33.54
ATOM	3225	O4	SO4	1001	7.429	28.930	21.367	1.00	32.87

DNA COORDINATES

		Atom Type	Resid	#	X	Y	Z	OCC	B
ATOM	3226	O3'	THY	3	37.257	37.479	7.626	1.00	62.88
ATOM	3227	P	THY	3	38.537	37.587	8.598	1.00	64.59
ATOM	3228	O1P	THY	3	39.744	37.500	7.737	1.00	65.36
ATOM	3229	O2P	THY	3	38.349	38.772	9.478	1.00	64.52
ATOM	3230	O5'	THY	3	38.465	36.284	9.516	1.00	61.39
ATOM	3231	C2'	THY	3	39.582	33.841	11.157	1.00	57.22

ATOM	3232	C5'	THY	3	37.215	35.787	9.985	1.00	58.94
ATOM	3233	C4'	THY	3	37.364	34.359	10.454	1.00	57.48
ATOM	3234	O4'	THY	3	38.030	33.610	9.411	1.00	57.98
ATOM	3235	C1'	THY	3	39.244	33.059	9.901	1.00	57.84
ATOM	3236	C3'	THY	3	38.209	34.160	11.712	1.00	55.51
ATOM	3237	O3'	THY	3	37.714	33.032	12.440	1.00	53.32
ATOM	3238	P	THY	4	37.453	33.144	14.024	1.00	51.06
ATOM	3239	O1P	THY	4	38.284	32.114	14.682	1.00	52.62
ATOM	3240	O2P	THY	4	37.572	34.555	14.460	1.00	52.47
ATOM	3241	O5'	THY	4	35.934	32.695	14.174	1.00	51.46
ATOM	3242	N1	THY	4	33.007	29.972	13.415	1.00	46.84
ATOM	3243	C6	THY	4	34.293	29.767	12.965	1.00	47.09
ATOM	3244	C2	THY	4	31.944	29.300	12.868	1.00	45.86
ATOM	3245	O2	THY	4	30.796	29.449	13.234	1.00	45.89
ATOM	3246	N3	THY	4	32.280	28.434	11.866	1.00	46.41
ATOM	3247	C4	THY	4	33.542	28.179	11.371	1.00	47.33
ATOM	3248	O4	THY	4	33.690	27.380	10.465	1.00	49.11
ATOM	3249	C5	THY	4	34.610	28.916	11.991	1.00	47.24
ATOM	3250	C2'	THY	4	33.891	30.788	15.545	1.00	50.03
ATOM	3251	C5'	THY	4	34.879	33.651	14.170	1.00	50.28
ATOM	3252	C4'	THY	4	33.674	33.079	14.873	1.00	49.97
ATOM	3253	O4'	THY	4	32.919	32.228	13.976	1.00	48.97
ATOM	3254	C1'	THY	4	32.790	30.920	14.512	1.00	47.73
ATOM	3255	C3'	THY	4	34.075	32.202	16.056	1.00	50.49
ATOM	3256	O3'	THY	4	33.236	32.403	17.179	1.00	50.67
ATOM	3257	P	THY	5	33.285	31.347	18.371	1.00	47.87
ATOM	3258	O1P	THY	5	34.541	30.575	18.215	1.00	48.85
ATOM	3259	O2P	THY	5	33.015	32.074	19.631	1.00	48.56
ATOM	3260	O5'	THY	5	32.072	30.374	18.051	1.00	49.19
ATOM	3261	N1	THY	5	31.213	27.155	16.419	1.00	58.66
ATOM	3262	C6	THY	5	32.482	27.691	16.481	1.00	59.82
ATOM	3263	C2	THY	5	30.878	26.224	15.460	1.00	60.12
ATOM	3264	O2	THY	5	29.775	25.706	15.384	1.00	61.69
ATOM	3265	N3	THY	5	31.896	25.911	14.590	1.00	60.92
ATOM	3266	C4	THY	5	33.180	26.422	14.589	1.00	60.86
ATOM	3267	O4	THY	5	33.980	26.063	13.733	1.00	62.48
ATOM	3268	C5	THY	5	33.467	27.375	15.633	1.00	60.58
ATOM	3269	C2'	THY	5	30.746	27.746	18.796	1.00	54.89
ATOM	3270	C5'	THY	5	30.759	30.895	17.870	1.00	52.14
ATOM	3271	C4'	THY	5	29.741	29.807	18.097	1.00	53.54
ATOM	3272	O4'	THY	5	29.757	28.886	16.980	1.00	54.95
ATOM	3273	C1'	THY	5	30.192	27.595	17.387	1.00	56.51
ATOM	3274	C3'	THY	5	30.042	28.976	19.338	1.00	53.67
ATOM	3275	O3'	THY	5	28.841	28.640	20.011	1.00	53.59
ATOM	3276	P	THY	6	28.902	27.677	21.286	1.00	55.49
ATOM	3277	O1P	THY	6	30.314	27.643	21.757	1.00	54.73
ATOM	3278	O2P	THY	6	27.825	28.072	22.235	1.00	56.13
ATOM	3279	O5'	THY	6	28.517	26.262	20.665	1.00	56.29
ATOM	3280	N1	THY	6	29.855	23.122	18.173	1.00	60.63
ATOM	3281	C6	THY	6	30.949	23.677	18.806	1.00	61.06
ATOM	3282	C2	THY	6	29.949	22.610	16.902	1.00	61.67
ATOM	3283	O2	THY	6	28.995	22.152	16.291	1.00	61.78
ATOM	3284	N3	THY	6	31.212	22.658	16.363	1.00	63.46
ATOM	3285	C4	THY	6	32.355	23.175	16.950	1.00	63.98
ATOM	3286	O4	THY	6	33.427	23.132	16.348	1.00	66.37
ATOM	3287	C5	THY	6	32.171	23.732	18.268	1.00	62.55
ATOM	3288	C2'	THY	6	28.701	23.043	20.380	1.00	58.13
ATOM	3289	C5'	THY	6	27.266	26.085	19.995	1.00	55.60

ATOM	3290	C4'	THY	6	27.031	24.624	19.695	1.00	56.65
ATOM	3291	O4'	THY	6	27.827	24.224	18.554	1.00	57.17
ATOM	3292	C1'	THY	6	28.559	23.051	18.868	1.00	58.86
ATOM	3293	C3'	THY	6	27.402	23.677	20.838	1.00	57.43
ATOM	3294	O3'	THY	6	26.423	22.658	21.005	1.00	57.14
ATOM	3295	P	THY	7	26.118	22.092	22.476	1.00	55.41
ATOM	3296	O1P	THY	7	27.388	21.574	23.052	1.00	55.46
ATOM	3297	O2P	THY	7	25.341	23.126	23.212	1.00	55.42
ATOM	3298	O5'	THY	7	25.155	20.856	22.209	1.00	54.29
ATOM	3299	N1	THY	7	28.804	18.991	19.952	1.00	50.01
ATOM	3300	C6	THY	7	29.541	19.632	20.927	1.00	49.74
ATOM	3301	C2	THY	7	29.235	18.962	18.632	1.00	49.72
ATOM	3302	O2	THY	7	28.630	18.401	17.735	1.00	49.11
ATOM	3303	N3	THY	7	30.418	19.620	18.403	1.00	49.95
ATOM	3304	C4	THY	7	31.199	20.284	19.331	1.00	50.77
ATOM	3305	O4	THY	7	32.238	20.836	18.973	1.00	52.95
ATOM	3306	C5	THY	7	30.695	20.267	20.688	1.00	50.49
ATOM	3307	C2'	THY	7	27.275	18.299	21.813	1.00	49.16
ATOM	3308	C5'	THY	7	24.826	20.456	20.880	1.00	51.47
ATOM	3309	C4'	THY	7	25.318	19.048	20.636	1.00	49.37
ATOM	3310	O4'	THY	7	26.467	19.074	19.756	1.00	49.04
ATOM	3311	C1'	THY	7	27.533	18.322	20.317	1.00	49.64
ATOM	3312	C3'	THY	7	25.759	18.341	21.914	1.00	48.18
ATOM	3313	O3'	THY	7	25.208	17.033	22.016	1.00	45.69
ATOM	3314	P	THY	8	25.223	16.282	23.434	1.00	43.16
ATOM	3315	O1P	THY	8	26.128	17.012	24.351	1.00	44.74
ATOM	3316	O2P	THY	8	23.837	16.004	23.867	1.00	44.40
ATOM	3317	O5'	THY	8	25.923	14.895	23.096	1.00	45.67
ATOM	3318	N1	THY	8	29.550	14.234	20.725	1.00	45.65
ATOM	3319	C6	THY	8	30.514	14.642	21.618	1.00	44.74
ATOM	3320	C2	THY	8	29.464	14.791	19.469	1.00	46.33
ATOM	3321	O2	THY	8	28.611	14.482	18.661	1.00	48.73
ATOM	3322	N3	THY	8	30.418	15.737	19.193	1.00	46.38
ATOM	3323	C4	THY	8	31.416	16.183	20.035	1.00	45.35
ATOM	3324	O4	THY	8	32.203	17.041	19.650	1.00	44.96
ATOM	3325	C5	THY	8	31.435	15.573	21.343	1.00	45.22
ATOM	3326	C2'	THY	8	28.573	12.869	22.592	1.00	46.80
ATOM	3327	C5'	THY	8	25.331	13.994	22.171	1.00	46.20
ATOM	3328	C4'	THY	8	26.346	12.982	21.695	1.00	46.45
ATOM	3329	O4'	THY	8	27.289	13.613	20.792	1.00	45.83
ATOM	3330	C1'	THY	8	28.598	13.170	21.103	1.00	46.11
ATOM	3331	C3'	THY	8	27.170	12.324	22.806	1.00	46.52
ATOM	3332	O3'	THY	8	27.137	10.893	22.783	1.00	46.89

WATER MOLECULE COORDINATES

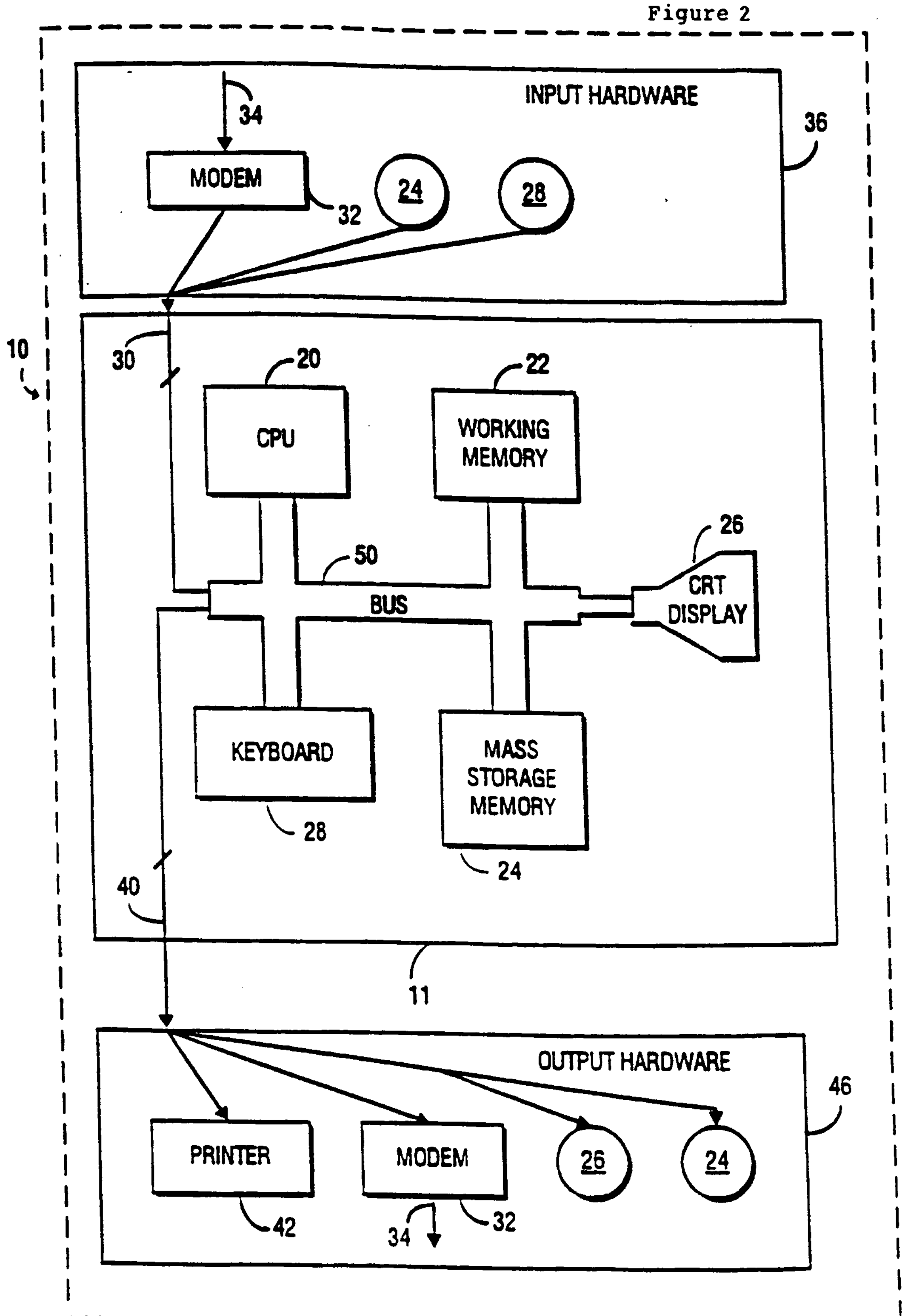
		Atom Type	Resid	#	X	Y	Z	OCC	B
ATOM	3333	OH2	TIP3	1	-0.245	23.385	32.975	1.00	19.18
ATOM	3334	OH2	TIP3	2	12.305	18.313	19.597	1.00	27.90
ATOM	3335	OH2	TIP3	3	16.363	43.283	27.772	1.00	24.59
ATOM	3336	OH2	TIP3	4	36.537	45.914	31.680	1.00	20.59
ATOM	3337	OH2	TIP3	5	17.542	27.937	8.465	1.00	18.37
ATOM	3338	OH2	TIP3	6	35.726	50.776	9.824	1.00	31.71
ATOM	3339	OH2	TIP3	7	20.453	38.335	27.173	1.00	47.06
ATOM	3340	OH2	TIP3	8	15.332	19.267	24.557	1.00	25.04
ATOM	3341	OH2	TIP3	9	31.258	50.933	30.493	1.00	29.38

ATOM	3342	OH2	TIP3	10	28.501	7.997	7.807	1.00	21.94
ATOM	3343	OH2	TIP3	11	24.624	24.209	25.328	1.00	24.23
ATOM	3344	OH2	TIP3	12	14.538	39.417	17.207	1.00	26.71
ATOM	3345	OH2	TIP3	13	19.304	29.672	7.885	1.00	17.01
ATOM	3346	OH2	TIP3	14	9.539	36.215	8.250	1.00	19.38
ATOM	3347	OH2	TIP3	15	22.976	53.935	15.769	1.00	19.99
ATOM	3348	OH2	TIP3	16	11.332	38.883	13.163	1.00	41.21
ATOM	3349	OH2	TIP3	17	44.389	17.456	4.710	1.00	25.71
ATOM	3350	OH2	TIP3	18	18.217	51.026	25.327	1.00	21.08
ATOM	3351	OH2	TIP3	19	52.875	8.529	0.460	1.00	38.69
ATOM	3352	OH2	TIP3	20	49.464	5.589	3.749	1.00	29.49
ATOM	3353	OH2	TIP3	21	18.312	39.750	29.166	1.00	35.93
ATOM	3354	OH2	TIP3	22	45.019	20.106	5.017	1.00	21.12
ATOM	3355	OH2	TIP3	23	0.745	18.945	33.170	1.00	25.64
ATOM	3356	OH2	TIP3	24	43.077	1.470	3.086	1.00	41.57
ATOM	3357	OH2	TIP3	25	32.242	40.177	37.162	1.00	30.45
ATOM	3358	OH2	TIP3	26	22.005	19.740	17.116	1.00	23.05
ATOM	3359	OH2	TIP3	27	23.883	51.464	21.877	1.00	39.16
ATOM	3360	OH2	TIP3	28	23.231	34.878	17.602	1.00	27.32
ATOM	3361	OH2	TIP3	29	16.275	41.943	30.227	1.00	44.09
ATOM	3362	OH2	TIP3	31	24.393	23.198	-0.349	1.00	34.79
ATOM	3363	OH2	TIP3	32	55.138	10.008	1.356	1.00	34.91
ATOM	3364	OH2	TIP3	33	8.529	32.844	5.639	1.00	48.78
ATOM	3365	OH2	TIP3	35	13.937	52.763	22.191	1.00	34.84
ATOM	3366	OH2	TIP3	36	17.459	5.667	9.998	1.00	37.45
ATOM	3367	OH2	TIP3	37	42.199	25.099	-1.836	1.00	37.69
ATOM	3368	OH2	TIP3	38	7.460	11.207	37.359	1.00	41.26
ATOM	3369	OH2	TIP3	39	24.315	32.263	19.069	1.00	27.49
ATOM	3370	OH2	TIP3	40	17.157	21.378	10.360	1.00	29.71
ATOM	3371	OH2	TIP3	41	13.157	9.144	28.767	1.00	32.39
ATOM	3372	OH2	TIP3	42	12.931	38.890	19.337	1.00	35.82
ATOM	3373	OH2	TIP3	43	38.696	43.515	31.888	1.00	28.12
ATOM	3374	OH2	TIP3	44	29.294	19.356	13.799	1.00	43.11
ATOM	3375	OH2	TIP3	45	9.044	7.812	9.252	1.00	19.18
ATOM	3376	OH2	TIP3	46	21.324	52.606	27.604	1.00	54.59
ATOM	3377	OH2	TIP3	47	30.914	34.967	12.824	1.00	25.06
ATOM	3378	OH2	TIP3	48	13.454	2.315	10.562	1.00	34.40
ATOM	3379	OH2	TIP3	49	28.876	32.558	13.029	1.00	51.94
ATOM	3380	OH2	TIP3	50	1.840	14.917	35.047	1.00	25.56
ATOM	3381	OH2	TIP3	51	20.036	5.057	8.439	1.00	38.71
ATOM	3382	OH2	TIP3	52	21.989	31.348	10.718	1.00	34.34
ATOM	3383	OH2	TIP3	53	22.314	46.201	35.658	1.00	33.59
ATOM	3384	OH2	TIP3	54	26.721	19.845	14.781	1.00	29.32
ATOM	3385	OH2	TIP3	55	21.199	6.956	15.517	1.00	31.86
ATOM	3386	OH2	TIP3	56	24.460	56.129	15.361	1.00	47.79
ATOM	3387	OH2	TIP3	57	24.841	34.491	13.673	1.00	35.87
ATOM	3388	OH2	TIP3	58	34.366	27.984	-0.318	1.00	26.26
ATOM	3389	OH2	TIP3	59	48.536	3.488	11.538	1.00	36.52
ATOM	3390	OH2	TIP3	60	2.038	28.336	33.590	1.00	32.11
ATOM	3391	OH2	TIP3	61	18.422	25.811	31.407	1.00	26.96
ATOM	3392	OH2	TIP3	62	12.957	44.530	11.249	1.00	28.06
ATOM	3393	OH2	TIP3	63	47.339	3.540	3.822	1.00	42.83
ATOM	3394	OH2	TIP3	64	11.061	16.825	19.834	1.00	26.76
ATOM	3395	OH2	TIP3	65	15.719	9.453	30.418	1.00	33.97
ATOM	3396	OH2	TIP3	66	45.394	-0.086	3.586	1.00	37.65
ATOM	3397	OH2	TIP3	67	33.010	41.548	3.551	1.00	53.15
ATOM	3398	OH2	TIP3	68	5.850	48.967	10.652	1.00	54.79
ATOM	3399	OH2	TIP3	69	17.164	56.234	13.372	1.00	23.47

ATOM	3400	OH2	TIP3	70	30.776	23.190	13.426	1.00	35.94
ATOM	3401	OH2	TIP3	71	39.550	3.505	-0.797	1.00	44.89
ATOM	3402	OH2	TIP3	72	11.418	30.014	18.681	1.00	37.07
ATOM	3403	OH2	TIP3	73	12.592	28.999	20.880	1.00	37.53
ATOM	3404	OH2	TIP3	74	54.478	6.360	11.185	1.00	42.03
ATOM	3405	OH2	TIP3	75	12.086	2.791	12.915	1.00	29.59
ATOM	3406	OH2	TIP3	76	18.225	19.519	33.978	1.00	33.10
ATOM	3407	OH2	TIP3	77	11.677	36.171	12.007	1.00	56.16
ATOM	3408	OH2	TIP3	78	11.319	35.115	15.313	1.00	35.91
ATOM	3409	OH2	TIP3	79	49.775	4.145	-0.325	1.00	63.48
ATOM	3410	OH2	TIP3	80	46.373	21.363	6.807	1.00	26.12
ATOM	3411	OH2	TIP3	81	18.126	35.806	20.605	1.00	29.66
ATOM	3412	OH2	TIP3	82	28.293	3.447	0.583	1.00	21.79
ATOM	3413	OH2	TIP3	83	20.086	4.628	14.855	1.00	44.92
ATOM	3414	OH2	TIP3	85	19.694	33.413	0.806	1.00	34.26
ATOM	3415	OH2	TIP3	87	17.814	5.041	25.621	1.00	45.94
ATOM	3416	OH2	TIP3	88	9.151	35.189	12.200	1.00	50.30
ATOM	3417	OH2	TIP3	89	28.063	25.834	6.403	1.00	47.14
ATOM	3418	OH2	TIP3	90	23.930	54.835	27.010	1.00	36.48
ATOM	3419	OH2	TIP3	91	8.080	25.210	6.084	1.00	33.01
ATOM	3420	OH2	TIP3	92	25.675	26.853	5.755	1.00	39.86
ATOM	3421	OH2	TIP3	93	36.215	33.769	7.228	1.00	24.13
ATOM	3422	OH2	TIP3	94	44.576	4.479	5.203	1.00	49.35
ATOM	3423	OH2	TIP3	95	8.686	33.376	8.329	1.00	28.75
ATOM	3424	OH2	TIP3	96	16.567	43.764	11.647	1.00	37.52
ATOM	3425	OH2	TIP3	97	18.639	37.102	28.670	1.00	34.49
ATOM	3426	OH2	TIP3	98	11.850	38.492	15.839	1.00	58.36
ATOM	3427	OH2	TIP3	99	1.757	17.697	30.552	1.00	30.16
ATOM	3428	OH2	TIP3	100	38.062	41.239	27.946	1.00	17.16
ATOM	3429	OH2	TIP3	101	27.889	50.445	37.057	1.00	48.61
ATOM	3430	OH2	TIP3	102	47.875	2.606	1.215	1.00	45.89
ATOM	3431	OH2	TIP3	103	57.882	18.168	8.130	1.00	45.09
ATOM	3432	OH2	TIP3	104	21.556	43.776	35.255	1.00	33.42
ATOM	3433	OH2	TIP3	105	22.140	30.473	5.457	1.00	39.79
ATOM	3434	OH2	TIP3	106	32.336	8.468	23.760	1.00	73.89
ATOM	3435	OH2	TIP3	107	51.548	8.278	-1.912	1.00	28.27
ATOM	3436	OH2	TIP3	108	8.860	13.655	39.162	1.00	33.15
ATOM	3437	OH2	TIP3	109	6.700	4.449	19.242	1.00	51.28
ATOM	3438	OH2	TIP3	110	33.801	29.559	25.988	1.00	53.24
ATOM	3439	OH2	TIP3	111	42.999	2.893	-1.302	1.00	46.52
ATOM	3440	OH2	TIP3	112	31.945	15.930	15.358	1.00	47.42
ATOM	3441	OH2	TIP3	113	22.230	16.440	-7.612	1.00	56.68
ATOM	3442	OH2	TIP3	115	13.726	39.997	22.208	1.00	31.56
ATOM	3443	OH2	TIP3	116	23.251	37.041	24.987	1.00	53.40
ATOM	3444	OH2	TIP3	117	23.611	32.166	12.751	1.00	38.21
ATOM	3445	OH2	TIP3	118	30.487	26.338	-0.700	1.00	31.83
ATOM	3446	OH2	TIP3	119	19.447	2.060	15.121	1.00	39.28
ATOM	3447	OH2	TIP3	120	24.042	51.710	8.456	1.00	39.94
ATOM	3448	OH2	TIP3	121	47.391	-0.070	5.383	1.00	37.69
ATOM	3449	OH2	TIP3	122	59.581	21.821	1.048	1.00	54.95
ATOM	3450	OH2	TIP3	123	9.207	34.806	15.904	1.00	31.85
ATOM	3451	OH2	TIP3	124	3.401	4.534	13.008	1.00	53.38
ATOM	3452	OH2	TIP3	125	11.114	48.341	33.295	1.00	43.92
ATOM	3453	OH2	TIP3	126	10.174	32.741	20.466	1.00	66.24
ATOM	3454	OH2	TIP3	128	16.410	45.512	26.424	1.00	35.46
ATOM	3455	OH2	TIP3	129	11.863	61.435	29.648	1.00	66.85
ATOM	3456	OH2	TIP3	130	33.387	55.608	7.433	1.00	64.07
ATOM	3457	OH2	TIP3	131	18.167	51.328	29.534	1.00	27.99

ATOM	3458	OH2	TIP3	132	16.147	45.753	6.715	1.00	54.98
ATOM	3459	OH2	TIP3	133	20.658	52.304	24.938	1.00	25.99
ATOM	3460	OH2	TIP3	134	44.627	9.499	-13.307	1.00	44.79
ATOM	3461	OH2	TIP3	135	64.095	6.945	12.329	1.00	44.41
ATOM	3462	OH2	TIP3	136	18.514	41.737	27.310	1.00	19.89
ATOM	3463	OH2	TIP3	137	42.275	19.609	-2.298	1.00	15.25
ATOM	3464	OH2	TIP3	139	14.970	49.971	28.272	1.00	35.15
ATOM	3465	OH2	TIP3	140	15.165	8.029	3.479	1.00	38.41
ATOM	3466	OH2	TIP3	141	17.347	7.548	21.016	1.00	36.09
ATOM	3467	OH2	TIP3	142	21.921	4.401	1.631	1.00	39.46
ATOM	3468	OH2	TIP3	143	23.711	49.091	33.933	1.00	39.80
ATOM	3469	OH2	TIP3	144	21.398	56.732	11.465	1.00	30.74
ATOM	3470	OH2	TIP3	145	15.424	25.910	28.153	1.00	28.23
ATOM	3471	OH2	TIP3	146	30.399	11.030	-7.068	1.00	50.79
ATOM	3472	OH2	TIP3	147	12.734	29.004	16.438	1.00	22.08
ATOM	3473	OH2	TIP3	148	53.920	5.003	16.906	1.00	54.39
ATOM	3474	OH2	TIP3	149	7.523	36.343	15.403	1.00	44.62
ATOM	3475	OH2	TIP3	150	14.223	30.953	15.400	1.00	37.15
ATOM	3476	OH2	TIP3	151	28.644	2.628	3.023	1.00	31.14
ATOM	3477	OH2	TIP3	152	15.963	9.043	22.893	1.00	26.75
ATOM	3478	OH2	TIP3	153	17.823	10.746	23.731	1.00	20.71
ATOM	3479	OH2	TIP3	154	29.179	54.461	32.613	1.00	68.03
ATOM	3480	OH2	TIP3	155	35.993	37.805	29.152	1.00	20.17
ATOM	3481	OH2	TIP3	156	53.831	24.063	9.859	1.00	49.86
ATOM	3482	OH2	TIP3	157	20.267	46.970	30.983	1.00	34.93
ATOM	3483	OH2	TIP3	158	32.383	43.988	6.930	1.00	39.67
ATOM	3484	OH2	TIP3	159	2.201	6.263	18.618	1.00	35.49
ATOM	3485	OH2	TIP3	160	48.626	11.397	-2.343	1.00	32.41
ATOM	3486	OH2	TIP3	161	21.594	8.868	-2.657	1.00	47.49
ATOM	3487	OH2	TIP3	162	21.981	51.645	6.828	1.00	36.67
ATOM	3488	OH2	TIP3	163	41.875	36.089	18.851	1.00	38.83
ATOM	3489	OH2	TIP3	164	39.302	39.590	11.776	1.00	50.01
ATOM	3490	OH2	TIP3	165	40.112	35.572	14.944	1.00	47.69
ATOM	3491	OH2	TIP3	166	39.529	30.929	22.535	1.00	41.91

Figure 2


INPUT HARDWARE
34
36
MODEM
32
24
28
10
30
20
22
CPU
WORKING
MEMORY
26
50
CRT
DISPLAY
BUS
KEYBOARD
MASS
STORAGE
MEMORY
28
24
40
11
OUTPUT HARDWARE
46
PRINTER
MODEM
26
24
42
34
32

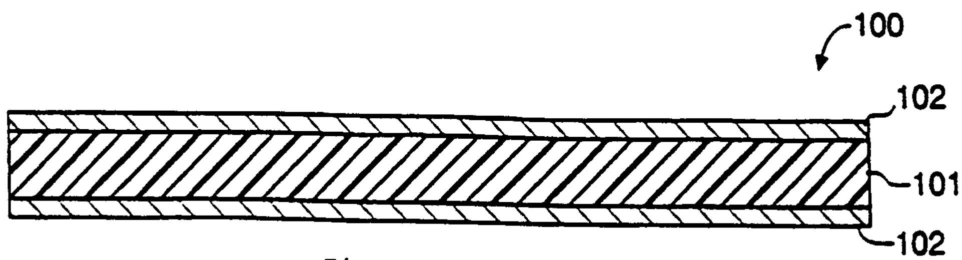


Figure 3

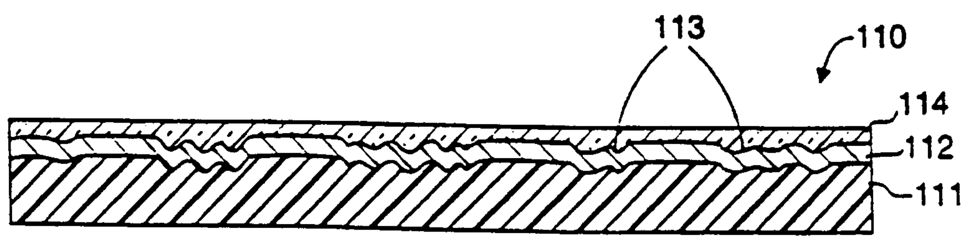


Figure 4

FIGURE 5

FIGURE 6

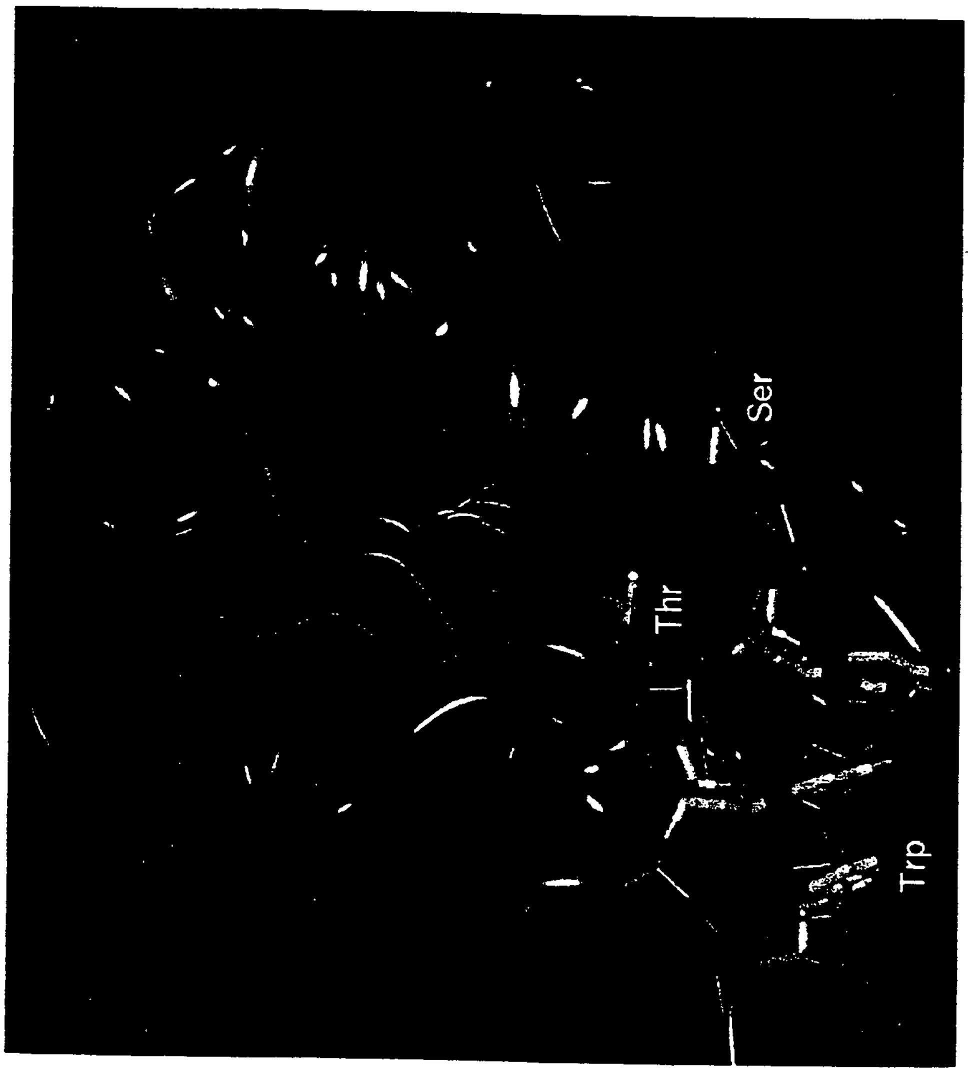


FIGURE 7

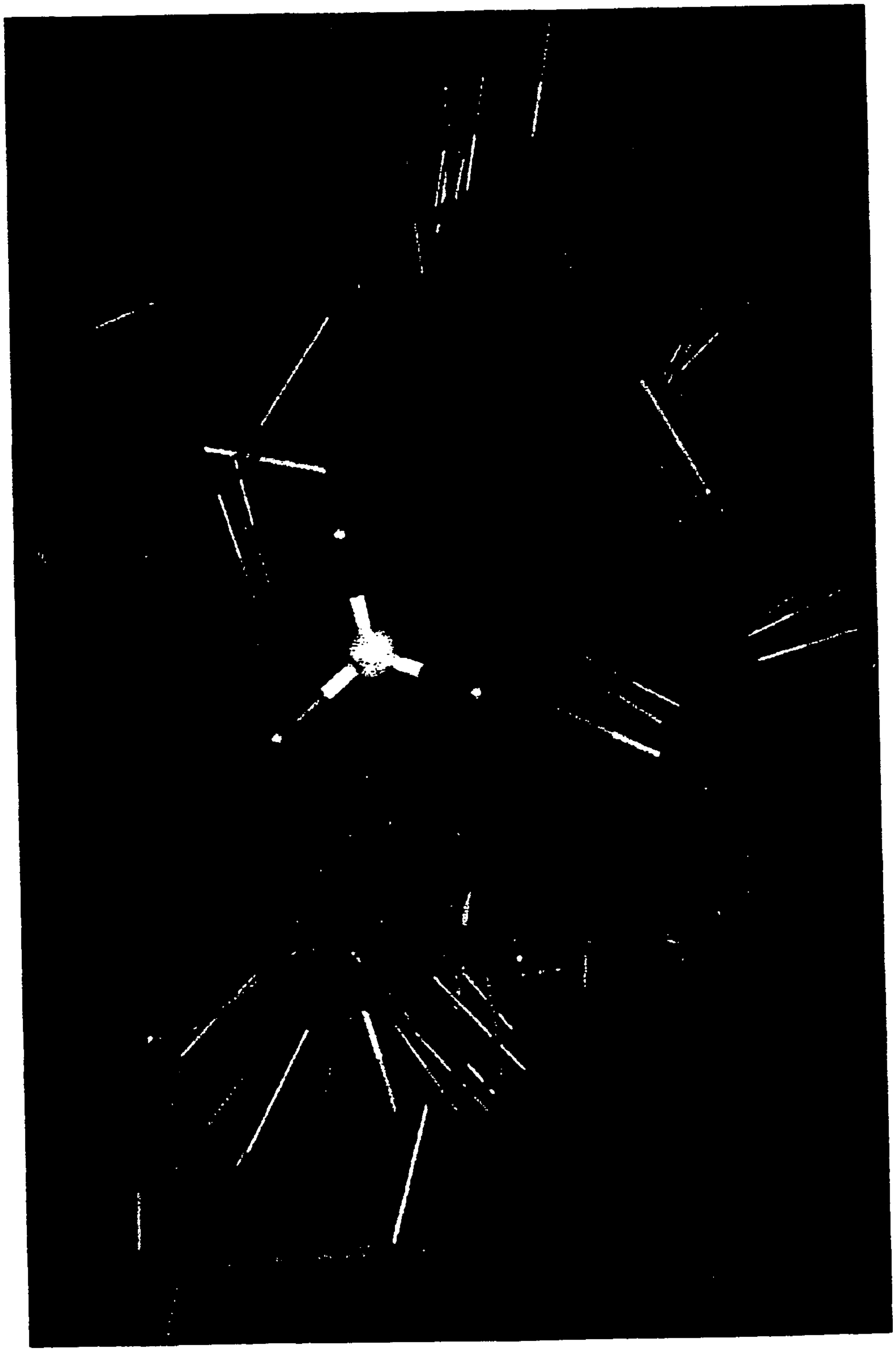


FIGURE 8

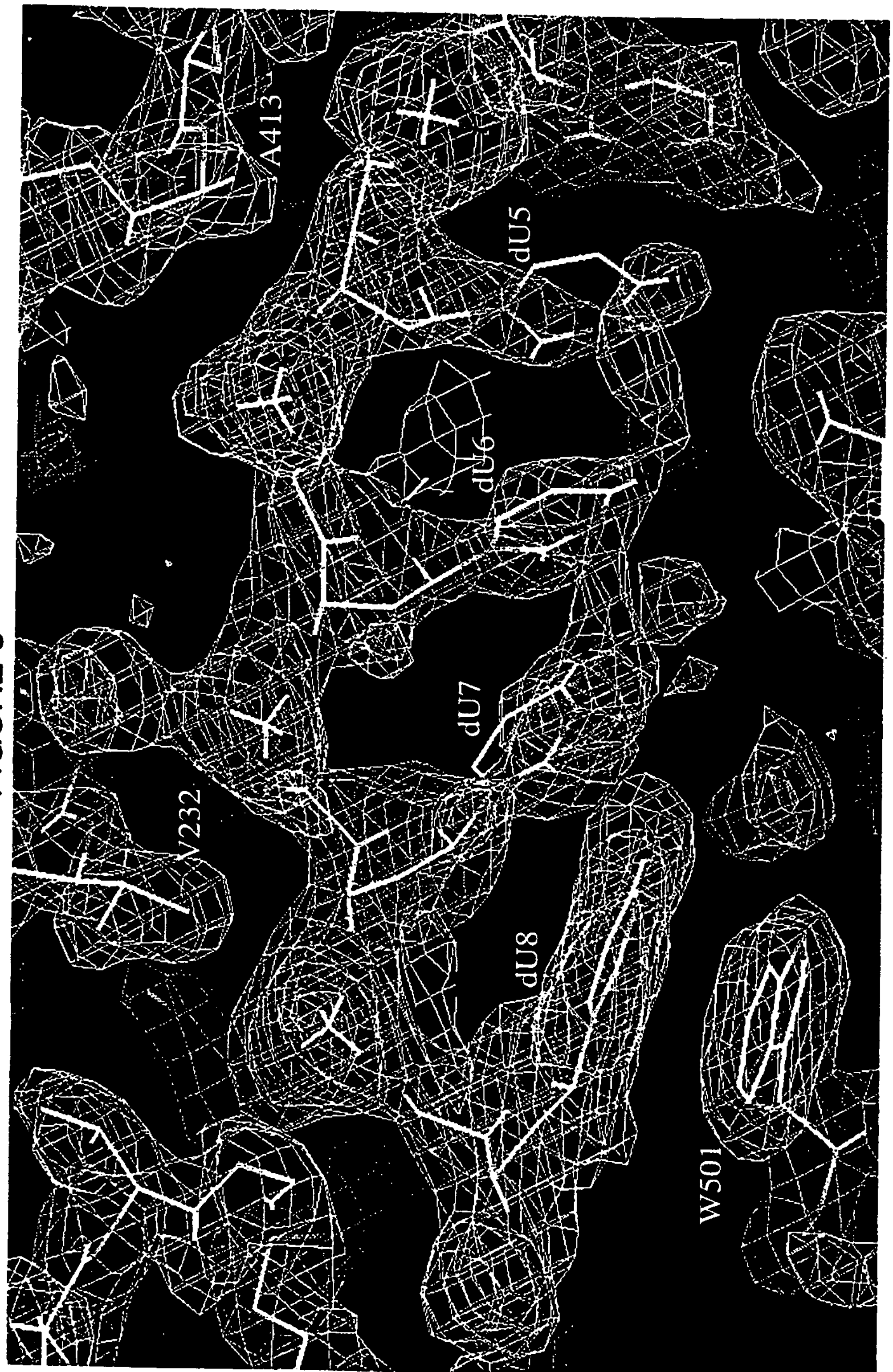


FIGURE 8

β1 α1

m*VDFIPVENLETTMRSPVFTDNS*SPPAVPQSFQVAHLHAPTGSGKSTKVPAAYAA 220

β2 α2 β3 β4 β5 α3

QGYKVLVLNPSVAATLGFGAYMSKAHGVDPNIRTGVRTITTGSPITYSTYGKFLADGGCS 280

β6 α4 α4A β7 β1'

GGAYDIIICDECHSTDATSILGIGTVLDQAETAGARLVVLATATPPGSVTVPHPNIEEVA 340

β1A' β1B' α1' β2' α2' β3'

LSTTGEIPFYGKAIPLEVIKGGRHLIFCHSKKKCDELAAKLVALGINAVAYYRGLDVSVI 400

β5' β6' β6A' β6B' α4'

PTSGDVVVVATDAL*MTG*FTGDFDSVIDCNTCVTQTVDFSLDPTFTIETTTLPQDAVSRTQ 460

β7' β8 α5 α6

RRGRTGRGKPGIYRFVAPGERPSGMFDSSVLCECYDAGCAWYELTPAETTVRLRAYMNTP 520

β9 α7 α8 α9

GLPVCQDHLEFWEGVFTGLTHIDAHFLSQTKQSGENFPYLVAYQATVCARAQAPPPSWDQ 580

α10

MWKCLIRLKPTLHGPTPLLYRLGAVQNEVTLTHPITKYIMTCMSAD*LEVVT*gsgshhhhhh 641

		I		Ia		II		III
NS3	204	APTGSGKSTK	(13)	VLNPSVAATLGF	(40)	DECHSTD	(25)	TATPPGSVTVPHPN
NPH-II	185	GGTGVGKTSQ	(28)	VILSLPRIALVR	(60)	DEVHEHD	(23)	TATLEDDRERLKVF
EIF-4A	63	AQSGTGKTGT	(19)	MLAPTRELALQI	(63)	DEADEML	(24)	SATMPNDVLEVTTK
PcrA	31	AGAGSGKTRV	(20)	AITFTNKAAREM	(150)	DEYQDTN	(19)	VGDADQSIYRWRGA
UvrD	30	AGAGSGKTRV	(20)	AVTFTNKAAREM	(150)	DEFQDTN	(19)	VGDDDQSIYGWRGA
Rep	22	AGAGSGKTRV	(20)	AVTFTNKAAAEM	(150)	DEYQDTN	(19)	VGDDDQSIYSWRGA

		IV?		V		VI
NS3	365	LIFCHSKKK	(36)	ATDALMTGFTGDFE	(32)	VSRTQRRGRTGRG
NPH-II	397	IVFVASVAQ	(43)	STPYLESSVTIRNV	(24)	SMRDQRKGRVGRV
EIF-4A	263	VIFCNTRRK	(43)	STDLLARGIDVQQV	(12)	EERRLAYVGITRA
PcrA	280	ILLEQNYRS	(273)	MTLHAAKGLEFPVV	(23)	EERRLAYVGITRA
UvrD	278	IRLEQNYRS	(271)	MTLHSAKGLEFPQV	(23)	EERRLAYVGVTRA
Rep	272	IKLEQNYRS	(275)	MTLHASKGLEFPYV	(22)	EERRLAYVGITRA

FIGURE 9B

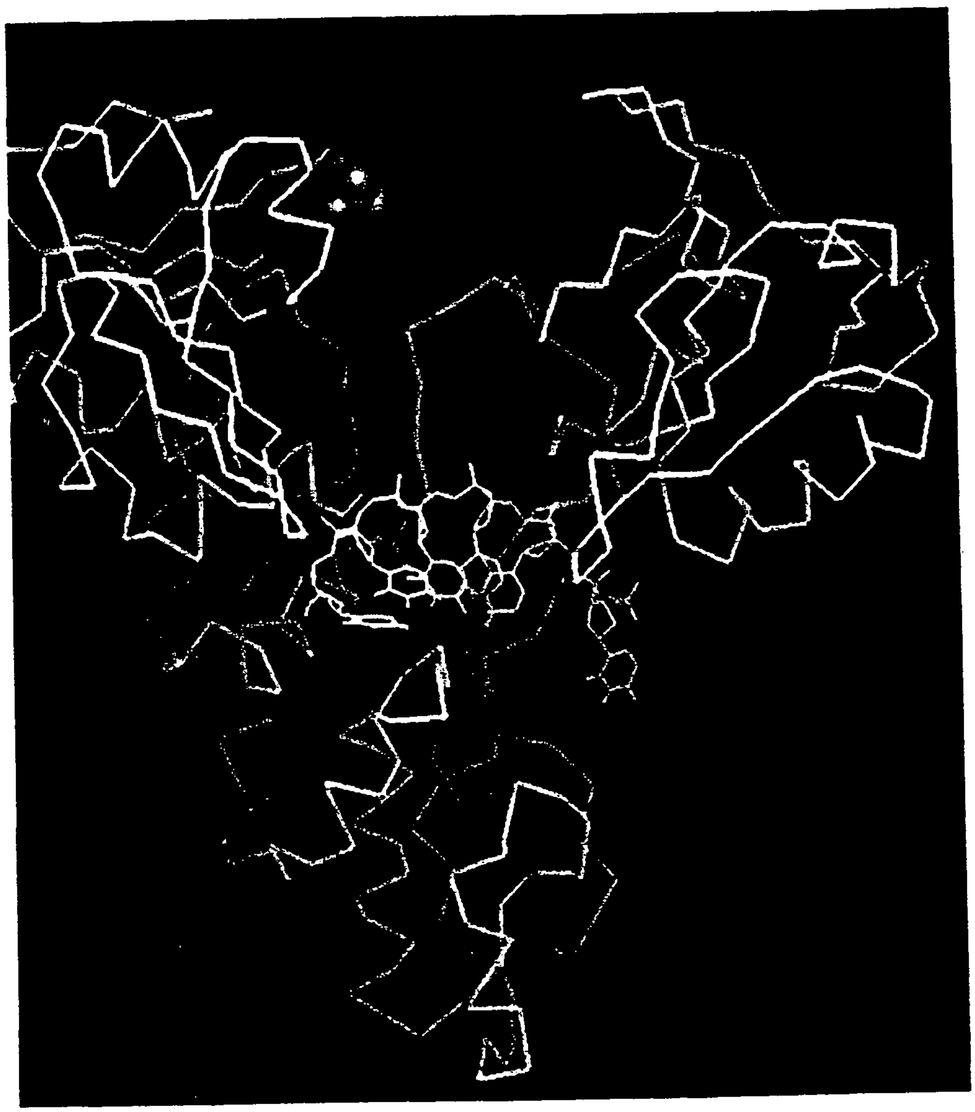


FIGURE 10

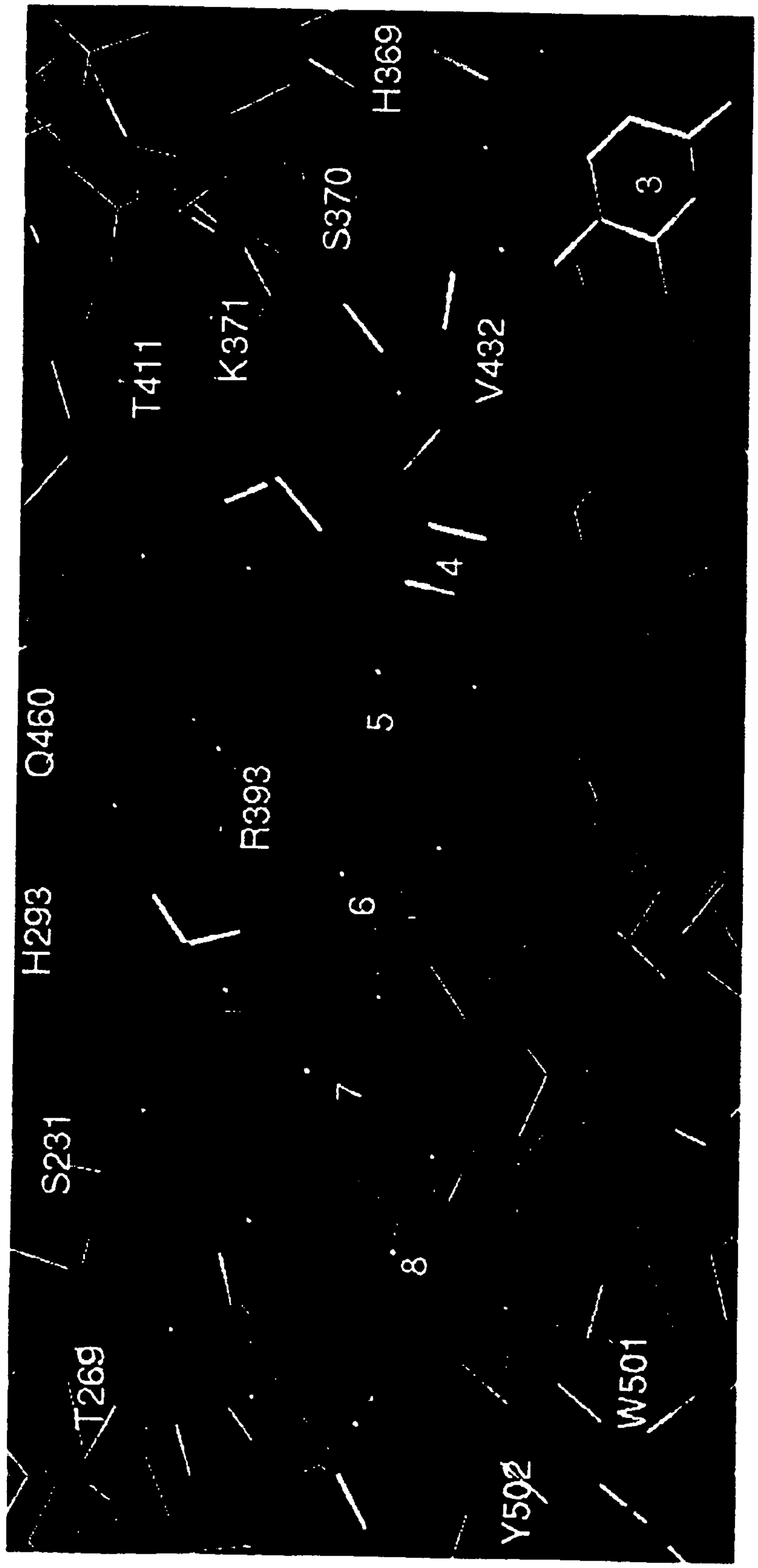

H369
S370
K371
T411
V432
3
4
5
Q460
R393
H293
6
7
S231
8
T269
W501
Y502

FIGURE 11A

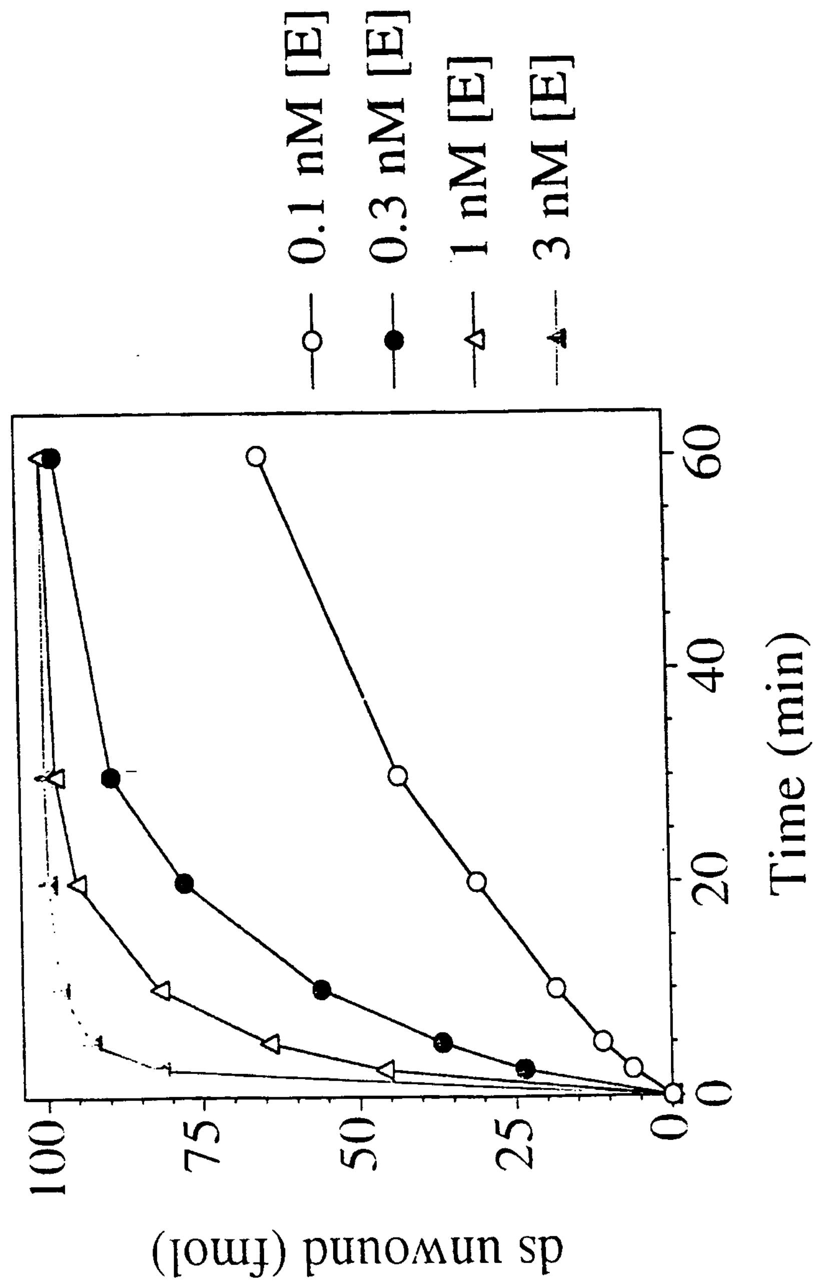

0.1 nM [E]
0.3 nM [E]
1 nM [E]
3 nM [E]
ds unwound (fmol)
0
25
50
75
100
Time (min)
0
20
40
60

FIGURE 11B

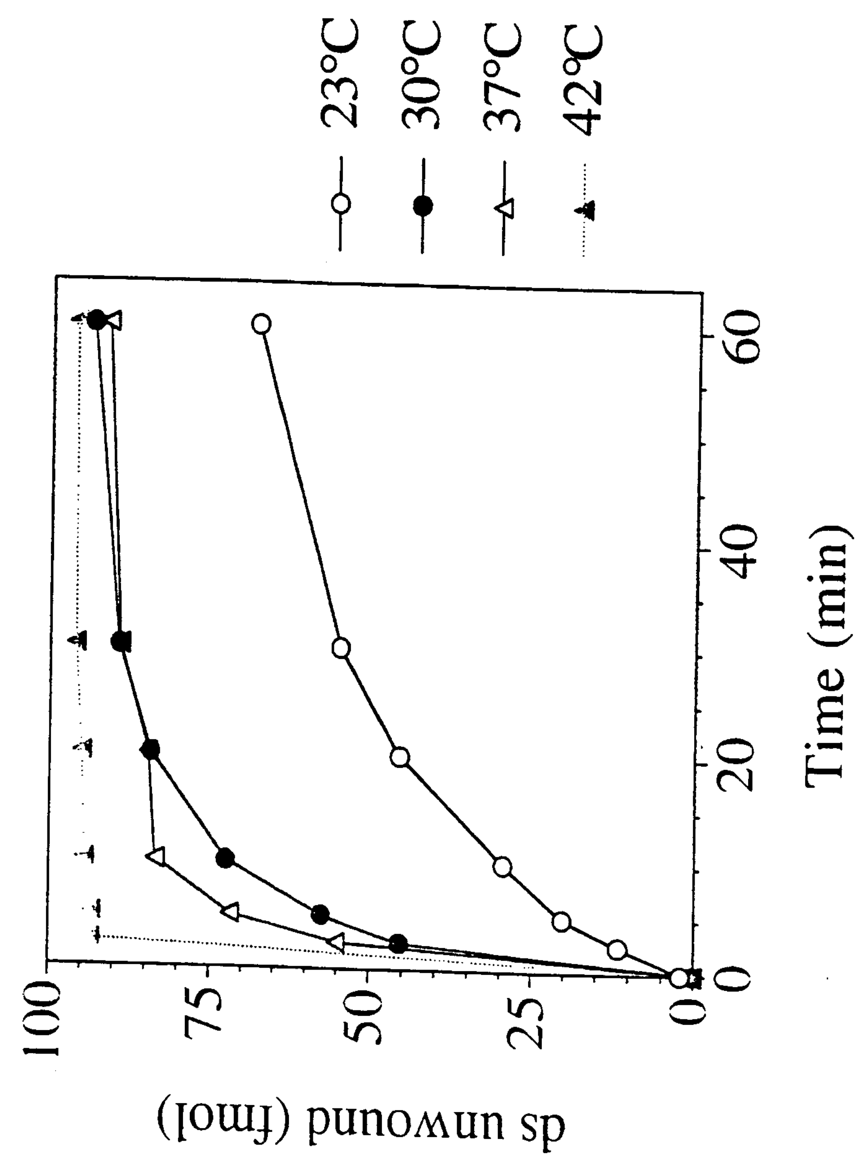


FIGURE 11C

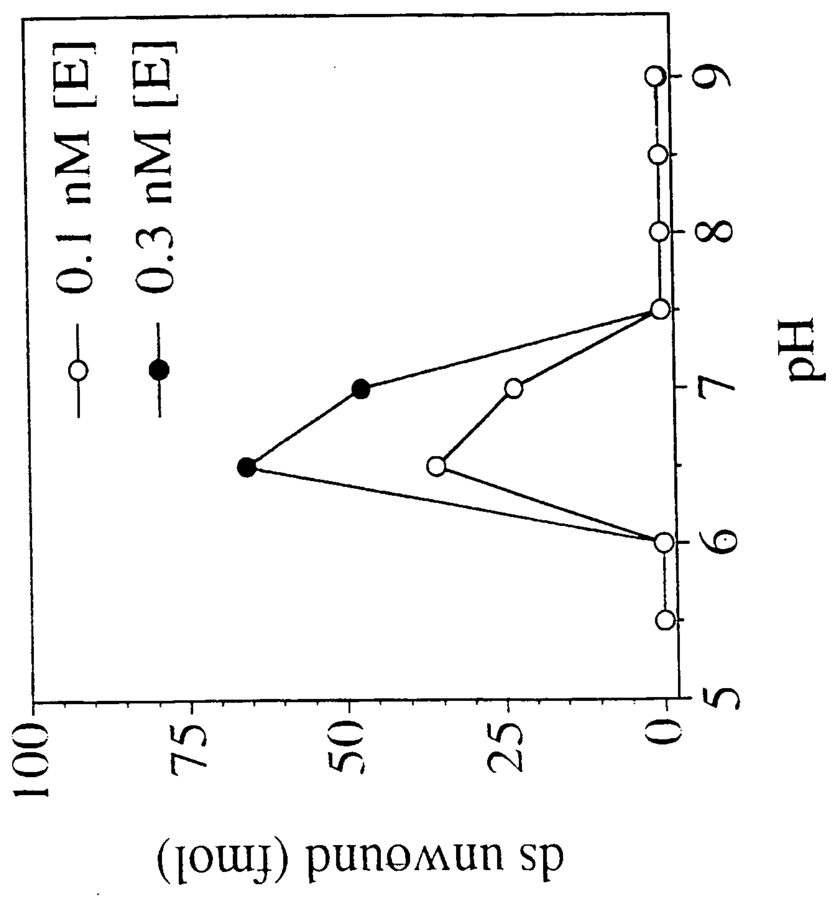


FIGURE 11D

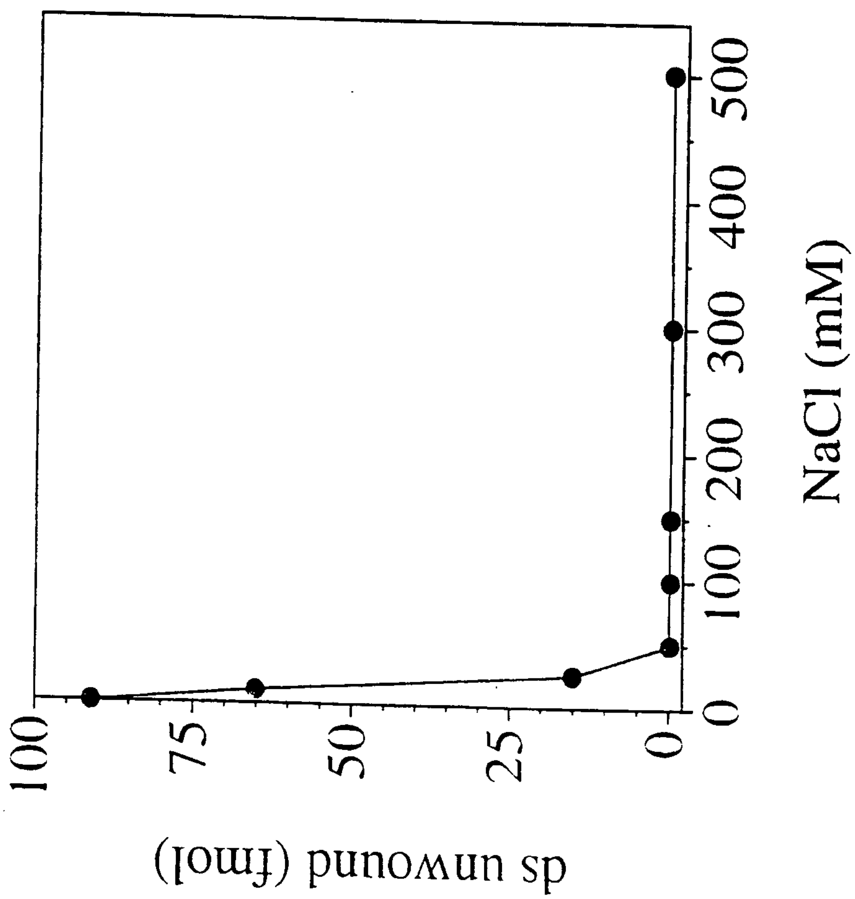


FIGURE 11E

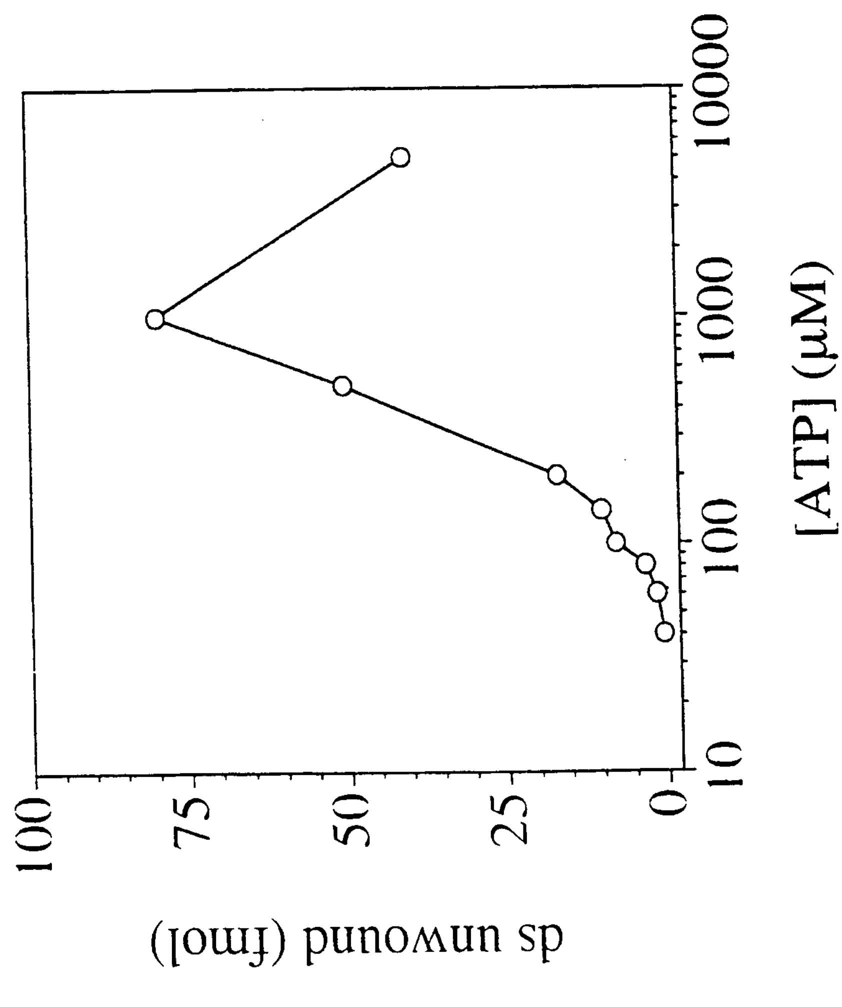


FIGURE 11F

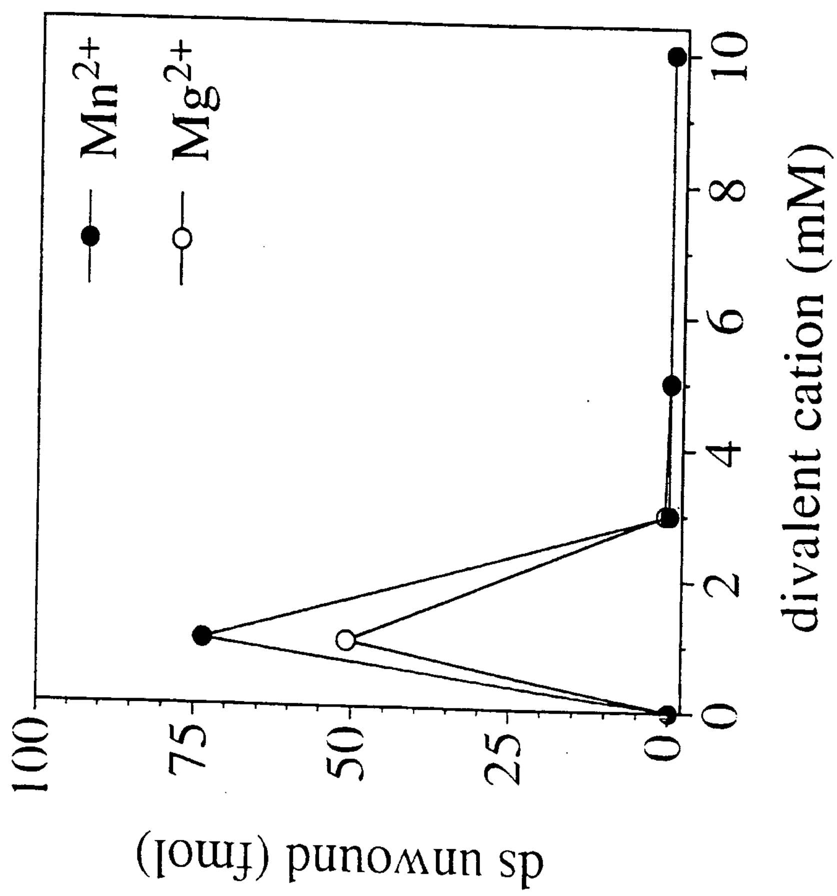

ds unwound (fmol)
100
75
50
25
0
0
2
4
6
8
10
divalent cation (mM)
Mn2+
Mg2+

FIGURE 12A

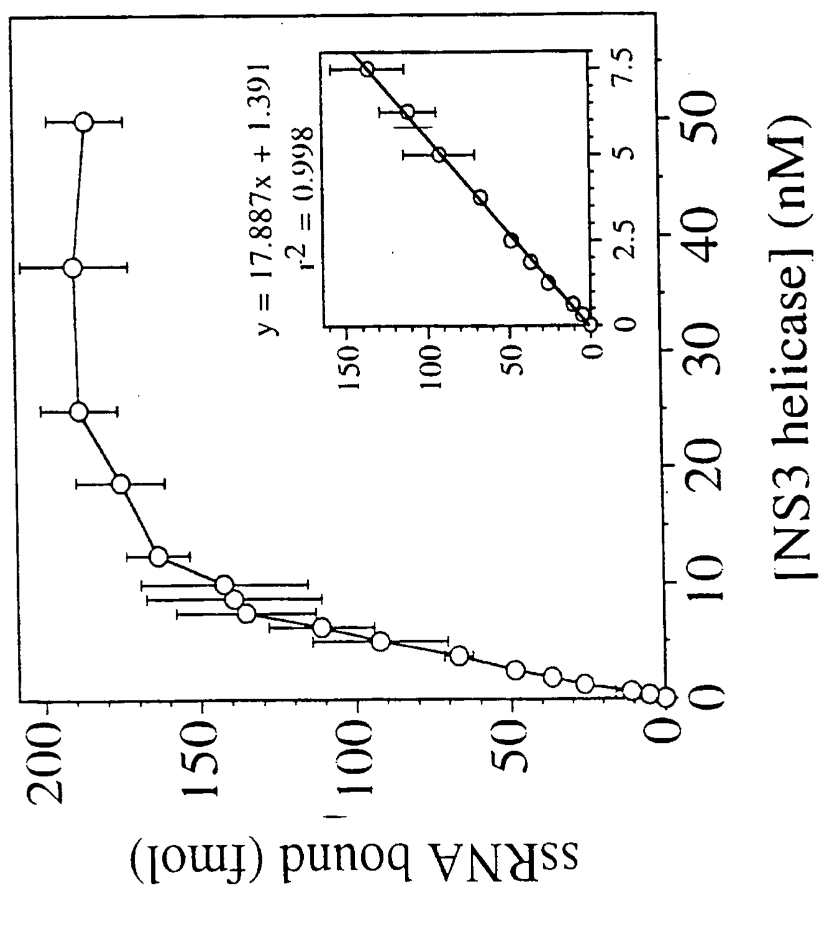

ssRNA bound (fmol)
[NS3 helicase] (nM)
y = 17.887x + 1.391
r^2 = 0.998
0
50
100
150
200
10
20
30
40
2.5
5
7.5

FIGURE 12B

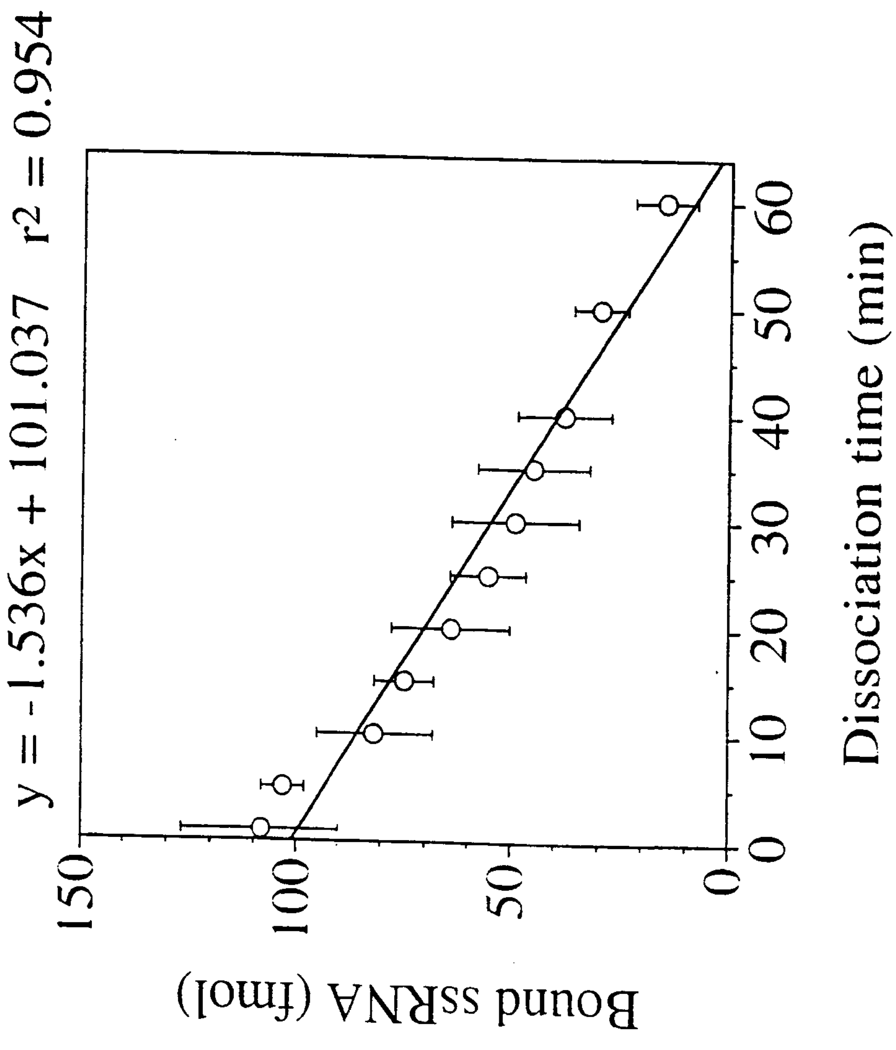

y = -1.536x + 101.037   r2 = 0.954
Bound ssRNA (fmol)
150
100
50
0
0
10
20
30
40
50
60
Dissociation time (min)

FIGURE 12C

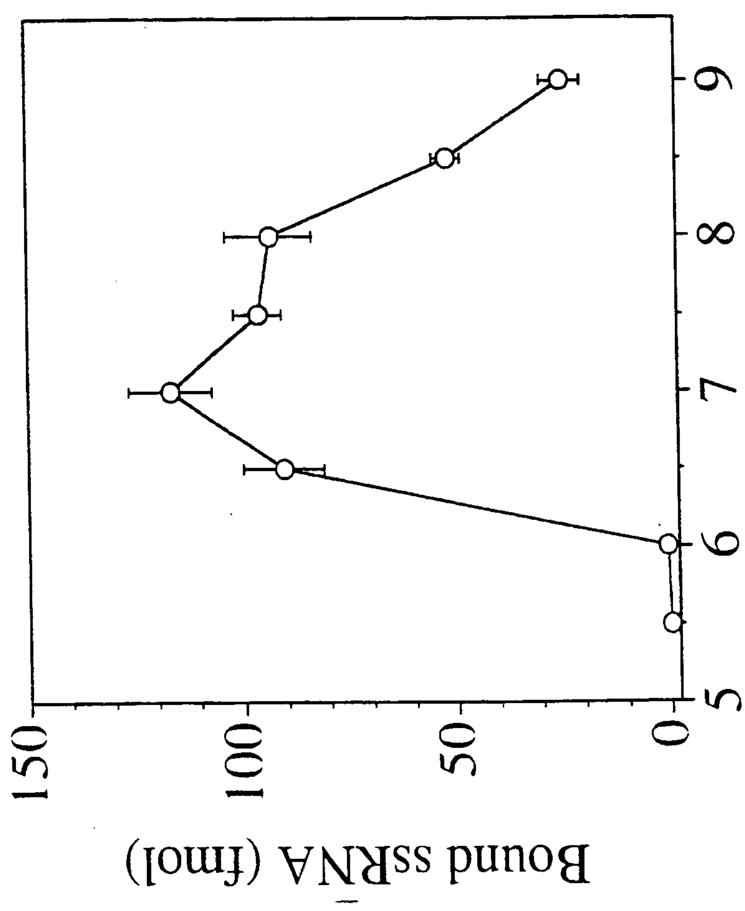


FIGURE 12D

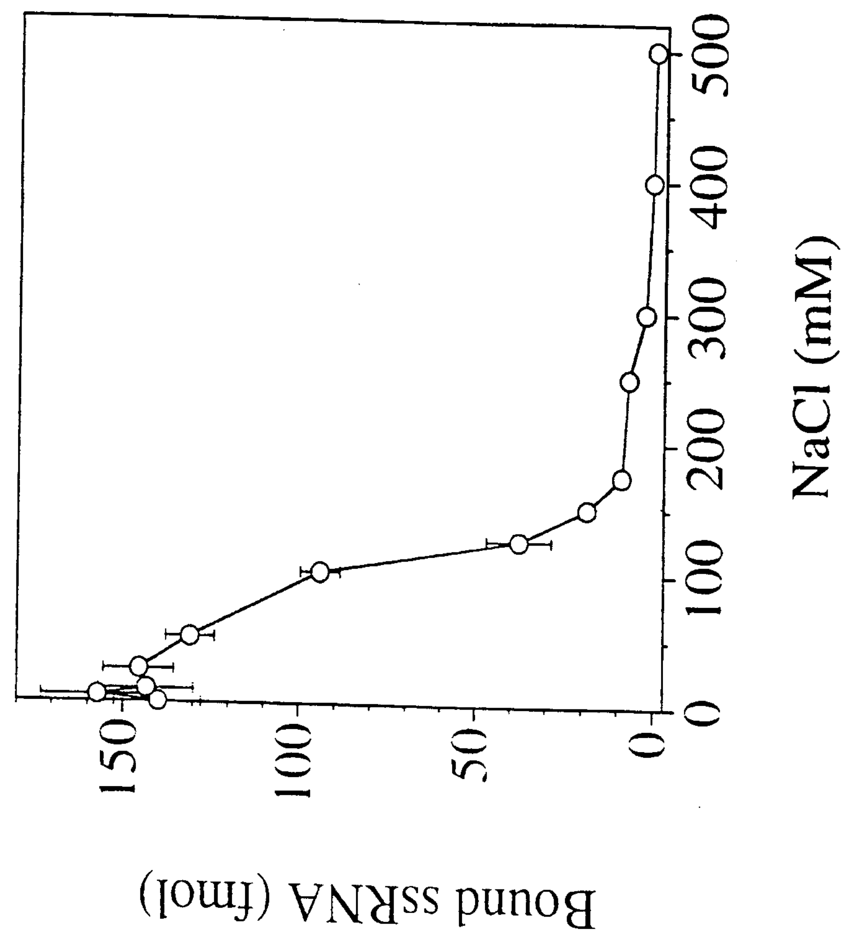


FIGURE 12E

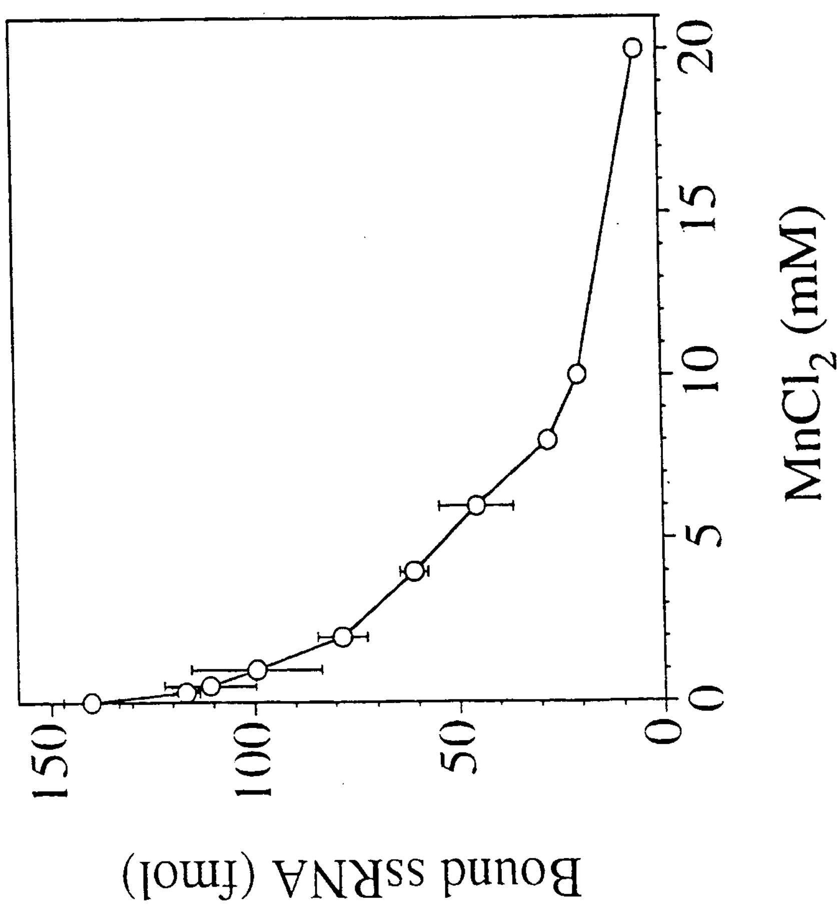


FIGURE 13A

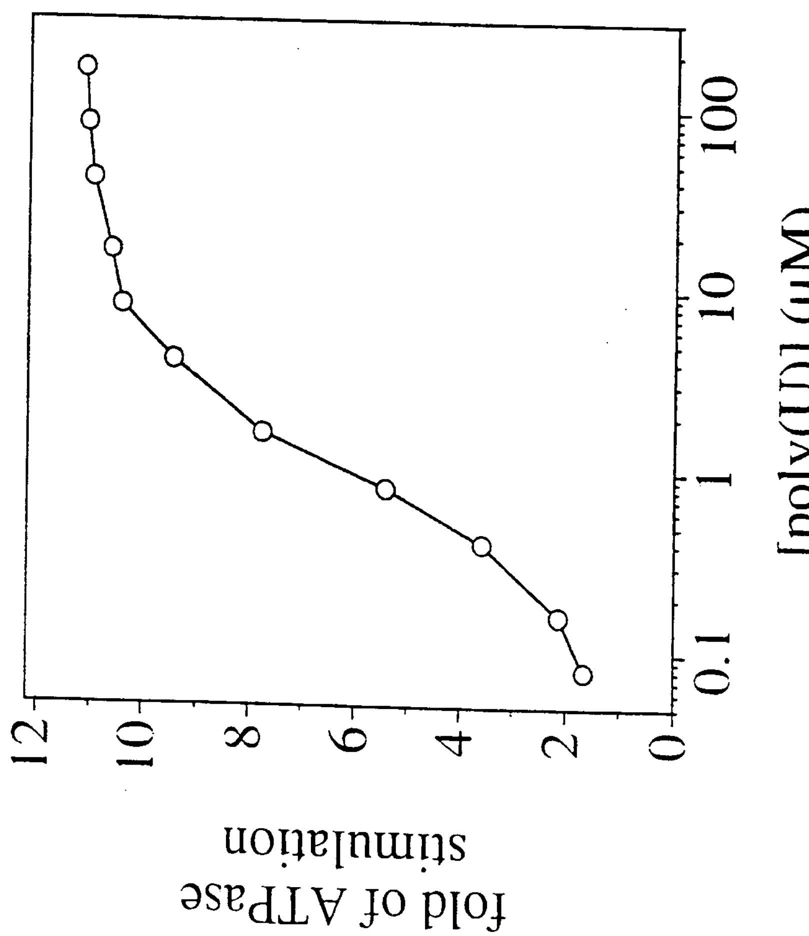
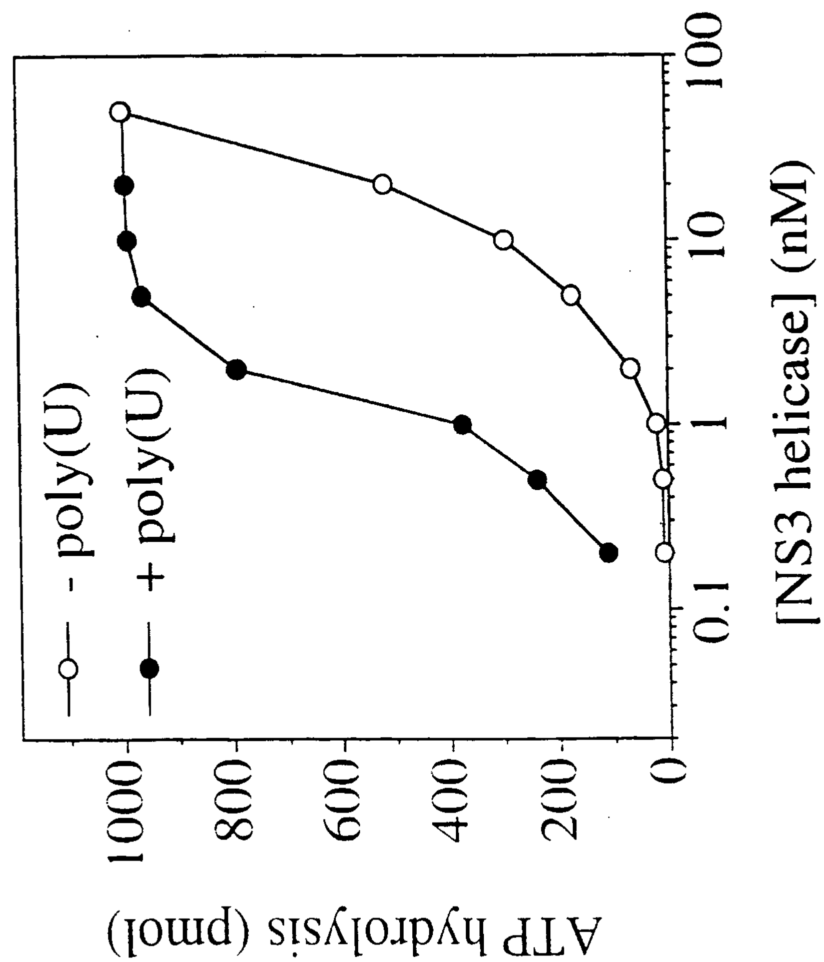


FIGURE 13B


- poly(U)
+ poly(U)
ATP hydrolysis (pmol)
0
200
400
600
800
1000
0.1
1
10
100
[NS3 helicase] (nM)

SEQUENCE LISTING

<110> Kim, Jospeh L

Morgenstern, Kurt A

Caron, Paul R

Lin, Chao

Vertex Pharmaceuticals Inc.

<120> CRYSTAL STRUCTURE OF THE HCV NS3 HELICASE DOMAIN

<130> Sequence listing for VPI/97-101

<140>

<141>

<150> 60/055,772

<151> 1997-08-13

<160> 4

<170> PatentIn Ver. 2.0

<210> 1

<211> 1932

<212> DNA

<213> Hepatitis C virus

<220>

<221> CDS

<222> (41)..(1896)

<223> Full length HCV NS3 coding sequence

<220>

<221> misc_feature

<222> (504)..(1896)

<223> Helicase domain

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atg gcg ccc atc acg gcg tac gcc cag cag acg aga ggc aag ctt ggg 48
Ala Pro Ile Thr Ala Tyr Ala Gln Gln Thr Arg Gly Lys Leu Gly
1 5 10 15

tgt ata atc acc agc ctg act ggc cgg gac aaa aac caa gtg gag ggt 96
Cys Ile Ile Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly
20 25 30

gag gtc cag atc gtg tca act gct acc caa acc ttc ctg gca acg tgc 144
Glu Val Gln Ile Val Ser Thr Ala Thr Gln Thr Phe Leu Ala Thr Cys
35 40 45

atc aat ggg gta tgc tgg act gtc tac cac ggg gcc gga acg agg acc 192
Ile Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Thr Arg Thr
50 55 60

atc gca tca ccc aag ggt cct gtc atc cag atg tat acc aat gtg gac 240
Ile Ala Ser Pro Lys Gly Pro Val Ile Gln Met Tyr Thr Asn Val Asp
65 70 75

caa gac ctt gtg ggc tgg ccc gct cct caa ggt tcc cgc tca ttg aca 288
Gln Asp Leu Val Gly Trp Pro Ala Pro Gln Gly Ser Arg Ser Leu Thr
80 85 90 95

ccc tgc acc tgc ggc tcc tcg gac ctt tac ctg gtt acg agg cac gcc 336
Pro Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala
100 105 110

gac gtc atc ccg gtt cgc cgt cgc ggt gat agc cgt ggt agc ctg ctg 384

Asp Val Ile Pro Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu

115 120 125

tct ccg cgt ccg att tcc tac ctg aaa ggc tcc tcg ggg ggt ccg ctg 432

Ser Pro Arg Pro Ile Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu

130 135 140

ttg tgc ccc gcg gga cac gcc gtg ggc cta ttc agg gcc gcg gtg tgc 480

Leu Cys Pro Ala Gly His Ala Val Gly Leu Phe Arg Ala Ala Val Cys

145 150 155

acc cgt gga gtg gcc aag gcg gtg gac ttt atc cct gtg gag aac ctg 528

Thr Arg Gly Val Ala Lys Ala Val Asp Phe Ile Pro Val Glu Asn Leu

160 165 170 175

gag acc acc atg cgt tcc ccg gtg ttc acg gac aac tcc tct cca cca 576

Glu Thr Thr Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro Pro

180 185 190

gct gtt ccc cag agc ttc cag gtg gcc cac ctg cat gct ccc acc ggc 624

Ala Val Pro Gln Ser Phe Gln Val Ala His Leu His Ala Pro Thr Gly

195 200 205

agt ggt aag agc acc aag gtc ccg gct gcg tac gca gcc cag ggc tac 672

Ser Gly Lys Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly Tyr

210 215 220

aag gtg ctg gtg ctc aac ccc tct gtt gct gca acg ctg ggc ttt ggt 720

Lys Val Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly

225 230 235

gct tac atg tcc aag gcc cat ggg gtc gat cct aat atc cgc acc ggt 768
Ala Tyr Met Ser Lys Ala His Gly Val Asp Pro Asn Ile Arg Thr Gly
240 245 250 255

gtg cgt aca att acc act ggc agc ccc atc acg tac tcc acc tac ggc 816
Val Arg Thr Ile Thr Thr Gly Ser Pro Ile Thr Tyr Ser Thr Tyr Gly
260 265 270

aag ttc ctt gcc gac ggc ggg tgc tca ggt ggc gct tat gat atc atc 864
Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile
275 280 285

att tgt gac gag tgc cac tcc acg gat gcc aca tcc atc ttg ggc atc 912
Ile Cys Asp Glu Cys His Ser Thr Asp Ala Thr Ser Ile Leu Gly Ile
290 295 300

ggc act gtc ctt gac caa gca gag act gcg ggg gcg aga ttg gtt gtg 960
Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val
305 310 315

ctc gcc act gct acc cct ccg ggc tcc gtc acg gta ccg cat cct aac 1008
Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn
320 325 330 335

atc gag gag gtt gct ctg tcc acc acc gga gag atc cct ttc tac ggc 1056
Ile Glu Glu Val Ala Leu Ser Thr Thr Gly Glu Ile Pro Phe Tyr Gly
340 345 350

aag gct atc ccc ctc gag gtg atc aag ggc ggc cgt cat ctc atc ttc 1104
Lys Ala Ile Pro Leu Glu Val Ile Lys Gly Gly Arg His Leu Ile Phe
355 360 365

tgt cac tca aag aag aag tgc gac gag ctc gcc gcg aag ctg gtc gca 1152
Cys His Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Val Ala
370 375 380

ttg ggc atc aat gcc gtg gcc tac tac cgc gga ctt gac gtg tct gtc 1200
Leu Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val
385 390 395

atc ccg acc agc ggc gat gtt gtc gtc gtg gcg acc gat gct ctc atg 1248
Ile Pro Thr Ser Gly Asp Val Val Val Val Ala Thr Asp Ala Leu Met
400 405 410 415

act ggc ttt acc ggc gac ttc gac tct gtg ata gac tgc aac acg tgt 1296
Thr Gly Phe Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys
420 425 430

gtc act cag aca gtc gat ttc agc ctt gac cct acc ttt acc att gag 1344
Val Thr Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu
435 440 445

aca acc acg ctc ccc cag gat gct gtc tcc agg act cag cgc cgt ggt 1392
Thr Thr Thr Leu Pro Gln Asp Ala Val Ser Arg Thr Gln Arg Arg Gly
450 455 460

cgt acc ggc cgt ggg aag cca ggc atc tac aga ttt gtg gca ccg ggg 1440
Arg Thr Gly Arg Gly Lys Pro Gly Ile Tyr Arg Phe Val Ala Pro Gly
465 470 475

gag cgc ccc tcc ggc atg ttc gac tcg tcc gtc ctc tgt gag tgc tat 1488
Glu Arg Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys Tyr
480 485 490 495

gac gcg ggc tgt gct tgg tat gag ctc acg ccg gcg gag act aca gtt 1536
Asp Ala Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Thr Val
500 505 510

cgt ctg cgc gcg tac atg aac acc ccg ggg ctt ccc gtg tgc cag gac 1584
Arg Leu Arg Ala Tyr Met Asn Thr Pro Gly Leu Pro Val Cys Gln Asp
515 520 525

cat ctt gaa ttt tgg gag ggc gtc ttt acg ggc ctc acc cat atc gat 1632
His Leu Glu Phe Trp Glu Gly Val Phe Thr Gly Leu Thr His Ile Asp
530 535 540

gcc cac ttt ctg tcc cag aca aag cag agt ggg gag aac ttt cct tac 1680
Ala His Phe Leu Ser Gln Thr Lys Gln Ser Gly Glu Asn Phe Pro Tyr
545 550 555

ctg gta gcg tac caa gcc acc gtg tgc gct cgt gcg caa gcc cct ccg 1728
Leu Val Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro
560 565 570 575

cca tcg tgg gac cag atg tgg aag tgt ttg atc cgc ctt aaa ccc acc 1776
Pro Ser Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr
580 585 590

ctc cat ggg cca aca ccg ctc ctg tac cgt ctg ggc gct gtt cag aat 1824
Leu His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn
595 600 605

gaa gtc acc ctg acg cac cca atc acc aaa tac atc atg aca tgc atg 1872
Glu Val Thr Leu Thr His Pro Ile Thr Lys Tyr Ile Met Thr Cys Met
610 615 620

tcg gcc gac ctg gag gtc gtc acg ggatctggct cgcatcatca tcatcatcac 1926

Ser Ala Asp Leu Glu Val Val Thr

625 630

taatag 1932

<210> 2

<211> 631

<212> PRT

<213> Hepatitis C virus

<400> 2

Ala Pro Ile Thr Ala Tyr Ala Gln Gln Thr Arg Gly Lys Leu Gly Cys

1 5 10 15

Ile Ile Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly Glu

20 25 30

Val Gln Ile Val Ser Thr Ala Thr Gln Thr Phe Leu Ala Thr Cys Ile

35 40 45

Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Thr Arg Thr Ile

50 55 60

Ala Ser Pro Lys Gly Pro Val Ile Gln Met Tyr Thr Asn Val Asp Gln

65 70 75 80

Asp Leu Val Gly Trp Pro Ala Pro Gln Gly Ser Arg Ser Leu Thr Pro

85 90 95

Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala Asp

100 105 110

Val Ile Pro Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu Ser

115 120 125

Pro Arg Pro Ile Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu Leu

130 135 140

Cys Pro Ala Gly His Ala Val Gly Leu Phe Arg Ala Ala Val Cys Thr

145 150 155 160

Arg Gly Val Ala Lys Ala Val Asp Phe Ile Pro Val Glu Asn Leu Glu

165 170 175

Thr Thr Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro Pro Ala

180 185 190

Val Pro Gln Ser Phe Gln Val Ala His Leu His Ala Pro Thr Gly Ser

195 200 205

Gly Lys Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly Tyr Lys

210 215 220

Val Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly Ala

225 230 235 240

Tyr Met Ser Lys Ala His Gly Val Asp Pro Asn Ile Arg Thr Gly Val

245 250 255

Arg Thr Ile Thr Thr Gly Ser Pro Ile Thr Tyr Ser Thr Tyr Gly Lys

260 265 270

Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile Ile

275 280 285

Cys Asp Glu Cys His Ser Thr Asp Ala Thr Ser Ile Leu Gly Ile Gly

290 295 300

Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val Leu
305 310 315 320

Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn Ile
325 330 335

Glu Glu Val Ala Leu Ser Thr Thr Gly Glu Ile Pro Phe Tyr Gly Lys
340 345 350

Ala Ile Pro Leu Glu Val Ile Lys Gly Gly Arg His Leu Ile Phe Cys
355 360 365

His Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Val Ala Leu
370 375 380

Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val Ile
385 390 395 400

Pro Thr Ser Gly Asp Val Val Val Val Ala Thr Asp Ala Leu Met Thr
405 410 415

Gly Phe Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys Val
420 425 430

Thr Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu Thr
435 440 445

Thr Thr Leu Pro Gln Asp Ala Val Ser Arg Thr Gln Arg Arg Gly Arg
450 455 460

Thr Gly Arg Gly Lys Pro Gly Ile Tyr Arg Phe Val Ala Pro Gly Glu
465 470 475 480

Arg Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys Tyr Asp

485 490 495

Ala Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Thr Val Arg

500 505 510

Leu Arg Ala Tyr Met Asn Thr Pro Gly Leu Pro Val Cys Gln Asp His

515 520 525

Leu Glu Phe Trp Glu Gly Val Phe Thr Gly Leu Thr His Ile Asp Ala

530 535 540

His Phe Leu Ser Gln Thr Lys Gln Ser Gly Glu Asn Phe Pro Tyr Leu

545 550 555 560

Val Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro Pro

565 570 575

Ser Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr Leu

580 585 590

His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn Glu

595 600 605

Val Thr Leu Thr His Pro Ile Thr Lys Tyr Ile Met Thr Cys Met Ser

610 615 620

Ala Asp Leu Glu Val Val Thr

625 630

<210> 3

<211> 8157

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Genetically engineered plasmid containing full-length HCV NS3 coding sequence

<400> 3

ttaatacgac tcactatagg ggaattgtga gcggataaca attcccctct agaaataatt 60

ttgtttaact ttaagaagga gatataccat ggcgcccatc acggcgtacg cccagcagac 120

gagaggcaag cttgggtgta taatcaccag cctgactggc cgggacaaaa accaagtgga 180

gggtgaggtc cagatcgtgt caactgctac ccaaaccttc ctggcaacgt gcatcaatgg 240

ggtatgctgg actgtctacc acggggccgg aacgaggacc atcgcatcac ccaagggtcc 300

tgtcatccag atgtatacca atgtggacca agaccttgtg ggctggcccg ctcctcaagg 360

ttcccgctca ttgacaccct gcacctgcgg ctcctcggac ctttacctgg ttacgaggca 420

cgccgacgtc atcccggttc gccgtcgcgg tgatagccgt ggtagcctgc tgtctccgcg 480

tccgatttcc tacctgaaag gctcctcggg gggtccgctg ttgtgccccg cgggacacgc 540

cgtgggccta ttcagggccg cggtgtgcac ccgtggagtg gccaaggcgg tggactttat 600

ccctgtggag aacctggaga ccaccatgcg ttccccggtg ttcacggaca actcctctcc 660

accagctgtt ccccagagct tccaggtggc ccacctgcat gctcccaccg gcagtggtaa 720

gagcaccaag gtcccggctg cgtacgcagc ccagggctac aaggtgttgg tgctcaaccc 780

ctctgttgct gcaacgctgg gctttggtgc ttacatgtcc aaggcccatg gggtcgatcc 840

taatatccgc accggtgtgc gtacaattac cactggcagc cccatcacgt actccaccta 900

cggcaagttc cttgccgacg gcgggtgctc aggtggcgct tatgatatca tcatttgtga 960

cgagtgccac tccacggatg ccacatccat cttgggcatc ggcactgtcc ttgaccaagc 1020

agagactgcg ggggcgagat tggttgtgct cgccactgct acccctccgg gctccgtcac 1080

ggtaccgcat cctaacatcg aggaggttgc tctgtccacc accggagaga tccctttcta 1140

cggcaaggct atcccccctcg aggtgatcaa gggcggccgt catctcatct tctgtcactc 1200

aaagaagaag tgcgacgagc tcgccgcgaa gctggtcgca ttgggcatca atgccgtggc 1260

ctactaccgc ggacttgacg tgtctgtcat cccgaccagc ggcgatgttg tcgtcgtggc 1320

gaccgatgct ctcatgactg gctttaccgg cgacttcgac tctgtgatag actgcaacac 1380

gtgtgtcact cagacagtcg atttcagcct tgaccctacc tttaccattg agacaaccac 1440

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aggcatctac agatttgtgg caccgggggа gcgcccctcc ggcatgttcg actcgtccgt 1560

ccctctgtgag tgctatgacg cgggctgtgc ttggtatgag ctcacgccgg cggagactac 1620

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tgcgcaagcc cctccgccat cgtgggacca gatgtggaag tgtttgatcc gccttaaacc 1860

caccctccat gggccaacac cgctcctgta ccgtctgggc gctgttcaga atgaagtcac 1920

cctgacgcac ccaatcacca aatacatcat gacatgcatg tcggccgacc tggaggtcgt 1980

cacgggatct ggctcgcatc atcatcatca tcactaatag aattcggatc cggctgctaa 2040

caaagcccga aaggaagctg agttggctgc tgccaccgct gagcaataac tagcataacc 2100

ccttggggcc tctaaacggg tcttgagggg ttttttgctg aaaggaggaa ctatatccgg 2160

atatcccgca agaggcccgg cagtaccggc ataaccaagc ctatgcctac agcatccagg 2220

gtgacggtgc cgaggatgac gatgagcgca ttgttagatt tcatacacgg tgcctgactg 2280

cgttagcaat ttaactgtga taaactaccg cattaaagct tatcgatacc gtcgacctcg 2340

aggggggggcc cggtacccaa ttcgccctat agtgagtcgt attacgcgcg ctcactggcc 2400

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gcacatcccc ctttcgccag ctggcgtaat agcgaagagg cccgcaccga tcgcccttcc 2520

caacagttgc gcagcctgaa tggcgaatgg gacgcgccct gtagcggcgc attaagcgcg 2580

gcgggtgtgg tggttacgcg cagcgtgacc gctacacttg ccagcgccct agcgcccgct 2640

cctttcgctt tcttcccttc ctttctcgcc acgttcgccg gctttccccg tcaagctcta 2700

aatcgggggc tccctttagg gttccgattt agtgctttac ggcacctcga ccccaaaaaa 2760

cttgattagg gtgatggttc acgtagtggg ccatcgccct gatagacggt ttttcgccct 2820

ttgacgttgg agtccacgtt ctttaatagt ggactcttgt tccaaactgg aacaacactc 2880

aaccctatct cggtctattc ttttgattta taagggattt tgccgatttc ggcctattgg 2940

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aaatacattc aaatatgtat ccgctcatga gacaataacc ctgataaatg cttcaataat 3120

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cggcattttg ccttcctgtt tttgctcacc cagaaacgct ggtgaaagta aaagatgctg 3240

aagatcagtt gggtgcacga gtgggttaca tcgaactgga tctcaacagc ggtaagatcc 3300

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gtggcgcggt attatcccgt attgacgccg ggcaagagca actcggtcgc cgcatacact 3420

attctcagaa tgacttggtt gagtactcac cagtcacaga aaagcatctt acggatggca 3480

tgacagtaag agaattatgc agtgctgcca taaccatgag tgataacact gcggccaact 3540

tacttctgac aacgatcgga ggaccgaagg agctaaccgc ttttttgcac aacatggggg 3600

atcatgtaac tcgccttgat cgttgggaac cggagctgaa tgaagccata ccaaacgacg 3660

agcgtgacac cacgatgcct gcagcaatgg caacaacgtt gcgcaaacta ttaactggcg 3720

aactacttac tctagcttcc cggcaacaat taatagactg gatggaggcg gataaagttg 3780

caggaccact tctgcgctcg gcccttccgg ctggctggtt tattgctgat aaatctggag 3840

ccggtgagcg tgggtctcgc ggtatcattg cagcactggg gccagatggt aagccctccc 3900

gtatcgtagt tatctacacg acggggagtc aggcaactat ggatgaacga aatagacaga 3960

tcgctgagat aggtgcctca ctgattaagc attggtaact gtcagaccaa gtttactcat 4020

atatacttta gattgattta aaacttcatt tttaatttaa aaggatctag gtgaagatcc 4080

tttttgataa tctcatgacc aaaatccctt aacgtgagtt ttcgttccac tgagcgtcag 4140

accccgtaga aaagatcaaa ggatcttctt gagatccttt ttttctgcgc gtaatctgct 4200

gcttgcaaac aaaaaaacca ccgctaccag cggtggtttg tttgccggat caagagctac 4260

caactctttt tccgaaggta actggcttca gcagagcgca gataccaaat actgtccttc 4320

tagtgtagcc gtagttaggc caccacttca agaactctgt agcaccgcct acatacctcg 4380

ctctgctaat cctgttacca gtggctgctg ccagtggcga taagtcgtgt cttaccgggt 4440

tggactcaag acgatagtta ccggataagg cgcagcggtc gggctgaacg gggggttcgt 4500

gcacacagcc cagcttggag cgaacgacct acaccgaact gagataccta cagcgtgagc 4560

tatgagaaag cgccacgctt cccgaaggga gaaaggcgga caggtatccg gtaagcggca 4620

gggtcggaac aggagagcgc acgagggagc ttccaggggg aaacgcctgg tatctttata 4680

gtcctgtcgg gtttcgccac ctctgacttg agcgtcgatt tttgtgatgc tcgtcagggg 4740

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 98/16879

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N9/90 C07K14/08 G06F17/50

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MORGENSTEIN, K. ET AL.: "Polynucleotide modulation of the protease, nucleoside triphosphate, and helicase activities of a hepatitis C virus NS3-NS4A complex isolated from transfected COS cells." JOURNAL OF VIROLOGY, vol. 71, no. 5, May 1997, pages 3767-75, XP002085174 cited in the application	1,2
Y	see the whole document	3-6
X	YAO, N. ET AL.: "Structure of the hepatitis C virus RNA helicase domain" NUTURE STRUCTURAL BIOLOGY, vol. 4, no. 6, June 1997, pages 463-7, XP002085175 cited in the application	7-24
Y	see the whole document	3-6

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search
11 December 1998

Date of mailing of the international search report
28/12/1998

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
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Fax: (+31-70) 340-3016

Authorized officer
SMALT, R

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 98/16879

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 15588 A (AZZO ALESSANDRA D ;RUDENKO GABRIELLE (US); HOL WIM G J (US)) 1 May 1997 see the whole document ---	7-23
X	WO 92 14211 A (UNIV LELAND STANFORD JUNIOR) 20 August 1992 see the whole document ---	24
A	BROWN, D.G. ET AL.: "Crystallography in the study of protein-DNA interactions." METHODS IN MOLECULAR BIOLOGY, vol. 56, 1996, pages 293-318, XP002087317 see the whole document ---	1-6,24
A	WO 97 12043 A (CHIRON CORP) 3 April 1997 see the whole document ---	
P,X	KIM, J.L. ET AL.: "Hepatitis virus NS3 RNA helicadse domain with a bound oligonucleotide: the crystal structure provides insight into the mode of unwinding." STRUCTURE, vol. 6, no. 1, 15 January 1998, pages 89-100, XP002085176 see the whole document ---	1-24
P,X	CHO, H.-S. ET AL.: "Crystal structure of RNA helicase from genotype 1b hepatitis C virus." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 24, 12 June 1998, pages 15045-52, XP002085177 see the whole document -----	7-24

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INTERNATIONAL SEARCH REPORT

Inte .ional application No.
PCT/US 98/ 16879

Box I Observations where certain claims were found unsearchable (Continuation f item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 7-23 in part
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 7-23 are directed to a program for computers and/or the presentation of information (Rule 39.1 (v and vi) PCT), the search has been carried out as far as possible.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

In...mation on patent family members

Internatic Application No
PCT/US 98/16879

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